UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

Date: October 15, 2014

SUBJECT: Difenoconazole. Request to Register New Multiple Active Ingredient (MAI) End-Use Product (Academy™ Fungicide) for New Post-Harvest Uses on Pome Fruit Group 11-10. Summary of Analytical Chemistry and Residue Data.

PC Code: 128847
Decision No.: 484399
Petition No.: 3F8209
Risk Assessment Type: Not Applicable
TXR No.: Not Applicable
MRID No.: See MRID Summary Table
Ver.Apr.08

DP Barcode: D417611
Registration No.: 100-RLEO (EPA File Symbol)
Regulatory Action: New Section 3 Registration
Case No.: 7014
CAS No.: 119446-68-3
40 CFR: §180.475

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Registration Division (7505P)

MRID Summary Table		
MRID No.	**Study Type**	**Comments**
49120717	860.1500 Apple and Pear – Foliar + Post-Harvest	New DER 49120717.der.docx

Executive Summary

Difenoconazole is a broad spectrum fungicide belonging to the triazole group of fungicides. It is currently registered in the U.S. for use as a seed treatment on a number of cereal grain crops, cotton, canola, and potato seed pieces and/or for multiple late-season foliar applications on numerous crops (including pome fruit group 11-10) and for post-harvest use on tuberous and corm vegetables subgroup 1C.

Tolerances for difenoconazole are currently established under 40 CFR §180.475. Tolerances for plant commodities are listed under §180.475(a)(1) and are expressed in terms of difenoconazole *per se*. Tolerances for livestock commodities are listed under §180.475(a)(2) and are expressed in terms of difenoconazole and its metabolite, CGA-205375. Tolerances are currently established in/on numerous crop commodities ranging from 0.01 ppm to 95 ppm and in meat, milk, and egg ranging from 0.01 ppm to 0.40 ppm. A tolerance in/on fruit, pome, group 11-10 is currently established at 1.0 ppm for multiple late-season foliar applications of difenoconazole. [Note: The current tolerance expression is in accordance with current guidance (Knizner, 5/27/09).]

Under PP#3F8209, Syngenta Crop Protection, LLC (hereafter referred to as Syngenta or petitioner) is requesting an increase in the currently established tolerances for residues of difenoconazole in/on the following:

Fruit, pome, group 11-10	from 1.0 ppm to 3.0 ppm
Apple, wet pomace	from 4.5 ppm to 7.5 ppm

In conjunction with PP#3F8209, Syngenta is requesting registration of a new multiple active ingredient (MAI) end-use product, Academy™ Fungicide (EPA File Symbol 100-RLEO), formulated as a flowable suspension concentrate (SC) containing both difenoconazole (20.9%; 2.06 lb ai/gal) and fludioxonil (12.5%; 1.23 lb ai/gal), for new post-harvest dip, drench, flood or spray uses of difenoconazole on pome fruit group 11-10. A single post-harvest application is proposed at 0.26 lb ai/100 gal for dip, drench or flood treatments and 0.26 lb ai/200,000 lb of fruit for spray treatment.

This review addresses the proposed uses for difenoconazole only.

The nature of the residue in primary crops is adequately understood based on acceptable plant metabolism studies reflecting foliar treatments on canola, grape, potato, tomato and wheat, and seed treatment in wheat. The HED Residues of Concern Knowledgebase Sub-committee (ROCKS) has determined that only the parent compound needs to be considered as a residue of concern in/on primary crop commodities for both tolerance enforcement and risk assessment (ROCKS Report Memo; DP#391350, 9/19/2011, W. Irwin).

The nature of the residue in livestock is adequately understood based on acceptable goat and hen metabolism studies. The HED ROCKS (ROCKS Report Memo; DP#391350, 9/19/2011, W. Irwin) has determined that the parent compound and the CGA-205375 metabolite are the residues of concern in livestock commodities for both tolerance enforcement and the risk assessment. In addition, metabolite OH-CGA-169374 should be considered as a residue of concern in milk for the dietary risk assessment. There is only one feedstuff associated with the proposed post-harvest uses of difenoconazole. Wet apple pomace is a carbohydrate

concentration (CC) which may be fed to dairy cattle. However, the dietary contribution from difenoconazole-treated wet apple pomace would constitute only a minor increase in the prior dietary burden calculation for dairy cattle and would not, by itself, warrant increasing currently established meat or milk tolerances.

An adequate tolerance enforcement method, Method AG-575B, is available for crop commodities. The method determines residues of difenoconazole *per se* in/on crop commodities by gas chromatography with nitrogen-phosphorus detection (GC/NPD). The method limits of quantitation (LOQs) are 0.01-0.05 ppm. A confirmatory GC method with mass-selective detection (MSD) is also available for crop commodities.

An adequate tolerance enforcement method, Method REM 147.07b, is available for livestock commodities. The method determines residues of difenoconazole and CGA-205375 in livestock commodities by liquid chromatography with tandem mass spectrometry detection (LC/MS/MS). The method LOQs are 0.01 ppm (for each analyte) for livestock tissues and 0.005 ppm (for each analyte) for milk. Adequate confirmatory methods, Method AG-544A and Method REM 147.06, are available for the determination of residues of difenoconazole and CGA-205375, respectively.

The submitted apple and pear magnitude of the residue data were evaluated under a joint review agreement between Health Canada's Pest Management Regulatory Agency (PMRA) and the USEPA. These data are deemed adequate to support the proposed post-harvest uses of difenoconazole on members of pome fruit group 11-10 and reflect the combined currently registered pre-harvest foliar use plus the proposed post-harvest uses. Since the maximum residues, highest average residues and recommended tolerances for apple and pear are within 5x, a crop group tolerance can be set for fruit, pome, group 11-10 and is recommended at 5.0 ppm based on the apple data reflecting the currently registered pre-harvest foliar and the proposed post-harvest drench uses and using the Organization for Economic Cooperation and Development (OECD) tolerance calculation procedures. The recommended tolerance in/on fruit, pome, group 11-10 is not the same as the petitioned-for tolerance increase.

Because difenoconazole is a triazole compound, HED generally requires that samples from any metabolism, field trial, and/or processing study be analysed for the triazole metabolites, triazolyl alanine, triazolyl acetic acid, and 1,2,4-triazole, for dietary risk assessment purposes. HED issued guidance on the residue chemistry data requirements for the triazole-based metabolites (DP# 327788, 4/25/06, M. Doherty). The apple and pear magnitude of the residue data submitted with this petition do not include analyses for the triazole metabolites which is acceptable given the proposed new uses. For the proposed post-harvest uses, anticipated residues of the triazole metabolites in/on pome fruit group 11-10 may be based on the incurred residues of parent adjusted for molecular weight. This topic will not be discussed further.

The previously submitted apple processing data indicate that residues of difenoconazole do not concentrate in juice but do concentrate in wet pomace. Based on the HAFT residues in/on apple (2.59 ppm for the post-harvest drench use) and the average processing factor for wet pomace (9.5x), the recommended tolerance in apple, wet pomace is 25 ppm. The recommended tolerance in apple, wet pomace is not the same as the petitioned-for tolerance increase.

A Codex maximum residue limit (MRL) for residues of difenoconazole in/on pome fruit is proposed at 0.8 mg/kg based on data reflecting foliar applications of difenoconazole. The Codex MRL would not be adequate to cover residues incurred from the proposed post-harvest uses in

the U.S.; therefore, harmonization with Codex is not possible at this time. A Mexican MRL has not been established for the requested crops. A Canadian MRL is established at 1 mg/kg in/on members of pome fruit group 11-10 (listed as individual crops); however, the submitted apple and pear magnitude of the residue data were evaluated under a joint review agreement between Health Canada's Pest Management Regulatory Agency (PMRA) and the USEPA and PMRA is expected to revise its MRL to harmonize with the U.S. recommended tolerance (5.0 ppm) at the end of their review. An International Residue Limit Status Sheet is attached in Appendix I.

Regulatory Recommendations and Residue Chemistry Deficiencies

HED has examined the residue chemistry database for difenoconazole. With regards to difenoconazole, pending submission of a revised Section F (see requirements under Proposed Tolerances) of the petition, HED has no objection to the registration of the new end-use product, Academy™ Fungicide (EPA File Symbol 100-RLEO), for the proposed post-harvest uses on pome fruit group 11-10 or increasing the established tolerances for residues of difenoconazole in/on the following:

Fruit, pome, group 11-10 ..... from 1.0 ppm to 5.0 ppm
Apple, wet pomace ..... from 4.5 ppm to 25 ppm

A human health risk assessment is forthcoming.

860.1550 Proposed Tolerances

Section F of the petition must be revised as follows. The recommended tolerances for residues of difenoconazole in/on fruit, pome, group 11-10 and apple, wet pomace are 5.0 ppm and 25 ppm, respectively. These are not the same as the petitioned-for tolerances which are deemed too low to cover difenoconazole residues which might be incurred from the proposed post-harvest use rates and techniques. See Table 8 for details.

Although both Syngenta and HED have used the OECD calculation procedures to determine tolerance levels for residues in/on fruit, pome, group 11-10, Syngenta's petitioned-for tolerance level is based on the combined residue data for both representative commodities (i.e., apples and pears) and some of the post-harvest application techniques but not all (i.e., dip and drench but not spray or dip+spray). However, HED, consistent with current practices, calculated separate tolerance levels for each representative commodity paired with each of the different post-harvest application techniques and then selected the maximum tolerance estimate from these combinations as the recommended level. Furthermore, PMRA is expected to use this same approach and revise its MRL in/on members of pome fruit group 11-10 to harmonize with the U.S. recommended tolerance (5.0 ppm) at the end of their review.

Syngenta did not provide any explanation for the petitioned-for level in apple, wet pomace. However, HED, consistent with current practices, calculated the recommended tolerance based on the highest average field trial (HAFT) residues in/on apple (2.59 ppm) and the average processing factor for wet pomace (9.5x).

Background

The chemical structure and nomenclature of difenoconazole and its regulated livestock metabolite CGA-205375, and the physicochemical properties of the technical grade of difenoconazole are presented in Tables 1 and 2.

Table 1. Difenoconazole Nomenclature.

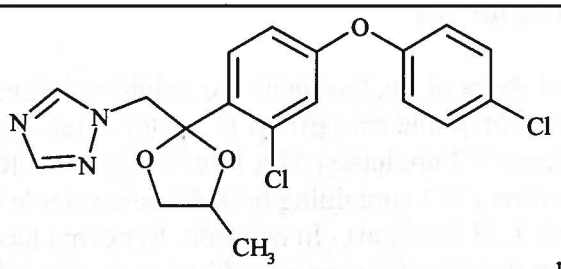
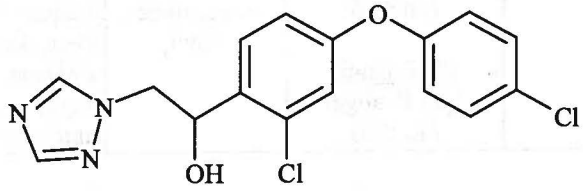
Chemical structure of parent	 mol. wt. 406.3
Common name	Difenoconazole
Company experimental name	CGA-169374
IUPAC name	1-[2-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-4-methyl-[1,3]dioxolan-2-ylmethyl]-1*H*-[1,2,4]triazole
CAS name	1-[[2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-yl]methyl]-1*H*-1,2,4-triazole
CAS registry number	119446-68-3
Chemical structure of CGA-205375 livestock metabolite	 mol. wt. 349.2

Table 2. Physicochemical Properties of Difenoconazole.

Parameter	Value	Reference
Melting point	78.6 °C	DP#s 172067 and 178394, 10/26/92, R. Lascola
pH	6-8 at 20 °C (saturated solution)	
Density	1.37 g/cm^3 at 20 °C	
Water solubility	3.3 ppm at 20 °C	
Solvent solubility	g/100 mL at 25 °C: n-hexane: 0.5 1-octanol: 35 toluene: 77 acetone: 88 ethanol: 89	
Vapor pressure	2.5 x 10^{-10} mm Hg at 25 °C	
Dissociation constant, pK_a	pure grade (99.3% ± 0.3%) difenoconazole in water (with 4% methanol) at 20°C is 1.1	DP# 375159, 5/26/10, B. Cropp-Kohlligian
Octanol/water partition coefficient, Log(K_{OW})	4.2 at 25 °C	DP#s 172067 and 178394, 10/26/92, R. Lascola

Table 2. Physicochemical Properties of Difenoconazole.		
Parameter	Value	Reference
UV/visible absorption spectrum	λ_{max} at about 200 and 238 nm (in methanol at 26 °C)	PMRA Proposed Regulatory Decision Document on Difenoconazole, 4/14/99 (PRDD99-01)

860.1200 Directions for Use

Under Section B of the petition, Syngenta has submitted directions for post-harvest dip, drench, flood, and spray uses on pome fruit group 11-10 for a new multiple active ingredient (MAI) end-use product, Academy™ Fungicide (EPA File Symbol 100-RLEO), formulated as a flowable suspension concentrate (SC) containing both difenoconazole (20.9%; 2.06 lb ai/gal) and fludioxonil (12.5%; 1.23 lb ai/gal). In addition, Syngenta has submitted a draft label with essentially the same use directions provided in Section B of the petition. The subject end-use product is identified in Table 3 and the use directions are summarized in Table 4.

Table 3. Summary of End-Use Products and Crops Under Consideration.					
Trade Name	EPA File Symbol	ai Content	Formulation Type	Target Crops	Source of Use Directions
Academy™ Fungicide	100-RLEO	Difenoconazole 2.06 lb ai/gal (20.9%) Fludioxonil 1.23 lb ai/gal (12.5%)	Flowable suspension concentrate (SC)	Pome Fruit Group 11-10: Apple; Azarole; Crabapple; Loquat; Mayhaw; Medlar; Pear; Pear, Asian; Quince; Quince, Chinese; Quince, Japanese; Tejocote and cultivars, varieties and/or hybrids of these.	Draft Label Dated 5/29/14

Table 4. Summary of Directions for Use of Difenoconazole.						
Appl. Timing, Type, and Equip.	Formulation [EPA File Symbol]	Max. Appl. Rate (lb ai/unit)	Max. No. Appl. per Season	Max. Seasonal Appl. Rate	PHI	Use Directions and Limitations
Pome Fruit Group 11-10 Post-Harvest Use						
Bin/Truck Drench or In-Line Dip/Drench or Flooder	2.06 lb ai/gal SC [100-RLEO]	0.26 lb ai/100 gal.	1 Do not make more than 1 post-harvest application of Academy to fruit.[1] Apply either once before storage or once after storage, just prior to marketing.	N/A	N/A	For in-line drench or dip applications, treat fruit for 15-30 seconds and allow fruit to drain. Fruit coatings may be applied separately after aqueous fungicide treatments.
In-Line Aqueous or Fruit Coating Spray Application		0.26 lb ai/200,000 lb of fruit				Mix the fungicide solution in an appropriate water, wax/oil emulsion, or aqueous dilution of a wax/oil emulsion for the crop being treated. Use T-jet, CDA, or similar application system.

PHI = Pre-Harvest Interval N/A = Not Applicable

1 Academy label specifies the following: Do not make more than two post-harvest applications of fludioxonil-containing products to the fruit.

Conclusions. The proposed use directions are adequate to allow evaluation of the residue chemistry data relative to the proposed uses of difenoconazole. HED notes that while data were generated reflecting a combination of pre-harvest foliar plus post-harvest dip plus spray treatments, the combined post-harvest dip plus spray treatment regimen was not a proposed use in this petition.

860.1300 Nature of the Residue - Plants

ROCKS Report Memo; DP#391350, 9/19/2011, W. Irwin

The nature of the residue in primary crops is understood based on acceptable plant metabolism studies reflecting foliar treatments in canola, grape, potato, tomato, and wheat. An acceptable wheat metabolism study reflecting seed treatment is also available. Based on the results of available plant metabolism studies, difenoconazole is metabolized in plants by the hydroxylation of the phenyl ring and/or cleavage of the dioxolane ring followed by cleavage of the carbon-carbon bridge between the phenyl and triazole rings.

The HED Residues of Concern Knowledgebase Sub-committee (ROCKS) has determined that only the parent compound needs to be considered as a residue of concern in/on primary crop commodities for both tolerance enforcement and risk assessment (ROCKS Report Memo; DP#391350, 9/19/2011, W. Irwin). Residues of metabolite CGA-205375 are higher in primary crops as the pre-harvest interval (PHI) increases; however, with the current/proposed crops/PHIs, the parent is sufficient to consider. If, additional uses on new crops with longer PHIs are proposed in the future, then the CGA-205375 metabolite may need to be considered for those uses/crops.

860.1300 Nature of the Residue - Livestock

ROCKS Report Memo; DP#391350, 9/19/2011, W. Irwin
Residue Chemistry Memo DP#s 172067 and 178394, 10/26/92, R. Lascola (MRID 42090042)

The nature of the residue in livestock is understood based on acceptable goat and hen metabolism studies. The HED Residues of Concern Knowledgebase Sub-committee (ROCKS) has determined that the parent compound (difenoconazole, CGA-169374) and the CGA-205375 metabolite are the residues of concern in livestock commodities for both tolerance enforcement and risk assessment (ROCKS Report Memo; DP#391350, 9/19/2011, W. Irwin). The metabolite CGA-205375 is the major residue in livestock and is considered to have toxicity comparable to the parent. In addition, metabolite OH-CGA-169374 (hydroxy-difenoconazole), which comprised 15.2% of the TRR in goat milk from the phenyl-labeled goat study (MRID 42090042; DP#s 172067 and 178394, 10/26/92, R. Lascola) when the combined residues of difenoconazole and the metabolite CGA-205375 comprised 29.9% of the TRR, should be considered as a residue of concern for risk assessment (ROCKS Report Memo; DP#391350, 9/19/2011, W. Irwin). Based on a simple ratio of TRR values, residues of OH-CGA-169374 in milk are expected to be approximately 0.5x the combined residues of difenoconazole and the metabolite CGA-205375. Therefore, based on available goat metabolism data, total residues of concern in milk for dietary risk assessments (parent, CGA-205375, and OH-CGA-169374), should be calculated by multiplying the tolerance in milk by 1.5x.

860.1340 Residue Analytical Methods

Crop Commodities

Residue Chemistry Memo DP# 356135, 9/17/09, B. Cropp-Kohlligian
Residue Chemistry Memo DP# 340379, 8/9/07, W. Wassell and M. Sahafeyan

Enforcement methods: An adequate enforcement method, GC/NPD method AG-575B, is available for the determination of residues of difenoconazole *per se* in/on plant commodities. An adequate enforcement method, GC/MSD method AG-676A, is also available for the determination of residues of difenoconazole *per se* in/on canola and barley commodities. A confirmatory method, GC/MSD method AG-676, is also available. The LOQs are 0.01-0.05 ppm.

Data collection methods: Apple and pear samples from the magnitude of the residue studies were analyzed for residues of difenoconazole using Analytical Method No. REM 147.08, a high performance liquid chromatography method with tandem mass spectrometry detection (LC/MS/MS). Acceptable method validation and concurrent recoveries were reported for apples and pear samples at fortification levels of 0.01-10 ppm, thus validating the methods. The limit of quantitation (LOQ; determined as the lowest level of method validation, LLMV) was 0.01 ppm for difenoconazole.

Livestock Commodities

Residue Chemistry Memo DP# 374898, 3/3/10, B. Cropp-Kohlligian
Residue Chemistry Memo DP#s 361054 and 362648, 9/17/09, B. Cropp-Kohlligian
Analytical Chemistry Branch Memo, 10/29/07, C. Stafford
Residue Chemistry Memo DP# 340379, 8/9/07, W. Wassell and M. Sahafeyan

Enforcement methods: An adequate tolerance enforcement method, Method REM 147.07b, is available for livestock commodities. The method determines residues of difenoconazole and

CGA-205375 in livestock commodities by liquid chromatography with tandem mass spectrometry detection (LC/MS/MS). The method LOQs are 0.01 ppm (for each analyte) for livestock tissues and 0.005 ppm (for each analyte) for milk. Adequate confirmatory methods, Method AG-544A and Method REM 147.06, are available for the determination of residues of difenoconazole and CGA-205375, respectively, in livestock commodities.

860.1360 Multiresidue Methods

Residue Chemistry Memo DP#s 172067 and 178394, 10/26/92, R. Lascola
Email from C. Stafford (Analytical Chemistry Branch) to B. Cropp-Kohlligian dated 9/2/09

Multiresidue methods (MRM) testing data (MRID 42090054) were previously submitted in conjunction with PP#2E4051 (DP#s 172067 and 178394, 10/26/92, R. Lascola). The study investigated the recovery of difenoconazole and its metabolites CGA-205374, CGA-205375, and CGA-189138 through the MRM methods of PAM Vol. I. Based on the study results, HED concluded, as did the petitioner, that the MRM methods were not likely to be appropriate for determining residues of difenoconazole and its related compounds in plant and livestock tissues. The study was forwarded to FDA for further review. Difenoconazole is not listed in the most recent PESTDATA (1999).

In contradiction to the MRM study evidence, Analytical Chemistry Branch (ACB) has noted (Email from C. Stafford (ACB) to B. Cropp-Kohlligian dated 9/2/09) that (1) FDA routinely monitors for difenoconazole by GC/MS using their current modified Luke procedures which are not in the published PAM I manual; (2) difenoconazole has also been tested through the QuEChERS (Quick, Easy, Cheap, Effective, Rugged, and Safe) method which is just beginning to be implemented in the FDA field labs using LC/MS/MS; and (3) the USDA-PDP program labs monitor for difenoconazole; the California Department of Food and Agriculture (CDFA), a participating laboratory, uses a multiresidue method with LC/MS analysis. Based on these facts, HED accepts that difenoconazole is recoverable through existing multiresidue methods, although the evidence is non-guideline and a conclusion concerning whether recovery is complete (>80%) cannot be reached. No additional MRM testing data are required at this time.

860.1380 Storage Stability

Crop Commodities

Residue Chemistry Memo DP#s 361054 and 362648, 9/17/09, B. Cropp-Kohlligian
Residue Chemistry Memo DP# 356135, 9/17/09, B. Cropp-Kohlligian
Residue Chemistry Memo DP# 340379, 8/9/07, W. Wassell and M. Sahafeyan

Samples of apples and pears from the new magnitude of the residue studies were stored frozen for up to 5.1 months prior to analysis for residues of parent. All samples were maintained frozen at the testing facility, during shipping to the laboratory, and at the laboratory until analysis. No new storage stability data for difenoconazole were submitted with the current petition. Based on previously submitted storage stability data, residues of difenoconazole have been shown to be stable under frozen conditions in/on representative raw agricultural commodities (RACs) for up to 1 year and in/on cotton seed, potato tuber, tomato, wheat forage, wheat grain, and wheat straw for up to 2 years.

The storage durations and conditions of samples from the magnitude of the residue studies submitted to support this petition are presented in Table 5.

Table 5. Summary of Storage Conditions and Durations of Samples from the Submitted Crop Field Trials.			
Matrix	Storage Temperature (°C)	Maximum Actual Storage Duration (months)	Interval of Demonstrated Storage Stability
Difenoconazole - Raw Agricultural Commodities			
Apple and pear	<-10	3.9-5.1	None provided with the current petition. Based on previously submitted storage stability data, when stored under frozen conditions, residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for up to one year. In addition, residues are stable for up to two years in/on cotton seed, potato tuber, tomato, wheat forage, wheat grain, and wheat straw.

Conclusions. With regards to difenoconazole, samples of apple and pear were stored frozen for up to 5.1 months prior to analysis for residues of difenoconazole. Available storage stability data indicate that residues of difenoconazole *per se* are stable under frozen conditions in/on all RACs for up to 1 year and in/on cotton seed, potato tuber, tomato, wheat forage, wheat grain, and wheat straw for up to 2 years. These data are deemed adequate to support the storage intervals and conditions of these samples for residues of difenoconazole.

Livestock Commodities

Residue Chemistry Memo DP# 375194, 6/17/10, B. Cropp-Kohlligian
Residue Chemistry Memo DP#s 361054 and 362648, 9/17/09, B. Cropp-Kohlligian
Residue Chemistry Memo DP# 340379, 8/9/07, W. Wassell and M. Sahafeyan

No new meat, milk, poultry, and egg data and/or supporting storage stability data for difenoconazole and/or its metabolites in/on livestock commodities were provided in the subject submissions.

Conclusions. With regards to residues of difenoconazole (CGA-169374) and its metabolite CGA-205375, the available storage stability data (47957201.der) and supplemental storage stability information provided in Report Number ABR-93012 (MRID 47957202) and Report Number 202/99 (MRID 47957203) are deemed adequate to support the storage intervals and conditions of samples collected from the cattle and poultry feeding studies previously submitted, reviewed by HED under PP# 6F7115 (D340379, 8/9/07, W. Wassell and M. Sahafeyan). The information in Report Numbers ABR-93012 and 202/99 is considered supplemental since study details and raw data were not provided.

With regards to the triazole metabolites, supporting storage stability data for residues of 1,2,4-triazole (1,2,4-T) are required to support the storage conditions (frozen) and intervals (up to 10 months) of livestock commodity samples collected for the cattle and poultry feeding studies. However, storage stability data for these compounds has been requested as part of the Human Health Aggregate Risk Assessment for the triazole metabolites (M. Doherty, *et al.*, 2/7/06) and these data, when submitted, are expected to satisfy storage stability data requirements for the subject petition.

860.1400 Water, Fish, and Irrigated Crops

There are no proposed uses that are relevant to this guideline topic.

860.1460 Food Handling

There are no proposed uses that are relevant to this guideline topic.

860.1480 Meat, Milk, Poultry, and Eggs

ROCKS Report Memo; DP#391350, 9/19/2011, W. Irwin
Residue Chemistry Memo PP#1E7852; DP# 389912, 5/30/12, B. Cropp-Kohlligian (meat and milk tolerances)
Residue Chemistry Memo PP#9F7676; DP# 378829, 2/23/11, B. Cropp-Kohlligian (egg tolerance)
Residue Chemistry Memo DP# 375194, 6/17/10, B. Cropp-Kohlligian
Residue Chemistry Memo DP# 340379, 8/9/07, W. Wassell and M. Sahafeyan
Residue Chemistry Memo DP#s 172067 and 178394, 10/26/92, R. Lascola

No new livestock feeding study data were submitted with the current petition. Adequate cattle and poultry feeding studies were previously submitted and are the basis for the currently established tolerances for difenoconazole residues of concern in meat, milk, and egg. There are no tolerances for difenoconazole residues of concern in poultry tissues. The currently established livestock commodity tolerances reflect the maximum reasonably balanced diets (MRBDs) for beef cattle (7.4 ppm), dairy cattle (2.8 ppm), poultry (0.11 ppm) and swine (0.09 ppm) for difenoconazole calculated using the most recent guidance on constructing MRBDs (ChemSAC memo, 6/30/08). See DP#s 378829 and 389912 for details.

There is a feedstuff associated with the proposed uses of difenoconazole for dairy cattle but not for beef cattle, poultry and swine. Wet apple pomace is a carbohydrate concentration (CC) with 40% dry matter (DM) which may be fed to dairy cattle at 10% of the diet. In accordance with ChemSAC recommendations concerning blended and nonblended feedstuffs (ChemSAC meeting minutes 8/26/09, 9/21/11 and 12/21/11), the difenoconazole residue estimates in/on wet apple pomace for dairy cattle MRBD calculations should be based on the median residue value for apple (highest median residue value was 1.22 ppm for dip + spray applications) and average concentration factor for wet apple pomace (9.5x). Wet apple pomace would contribute 2.9 ppm to the dairy cattle MRBD. In the prior dairy cattle MRBD calculation, the CC contribution was from processed potato waste which contributed 2.6 ppm to the dairy cattle MRBD. Hence, the dietary contribution from difenoconazole-treated wet apple pomace would constitute only a minor increase in the prior dairy cattle MRBD calculation and would not, by itself, warrant increasing currently established meat or milk tolerances.

Conclusions. There is a feedstuff associated with the proposed post-harvest uses of difenoconazole for dairy cattle but not for beef cattle, poultry and swine. Wet apple pomace is a carbohydrate concentration (CC) which may be fed to dairy cattle. However, the dietary contribution from difenoconazole-treated wet apple pomace would constitute only a minor increase in the prior maximum reasonably balanced diet calculation for dairy cattle and would not, by itself, warrant increasing currently established meat or milk tolerances.

860.1500 Crop Field Trials
49120717.der.docx (apple and pear post-harvest uses)

Apple and Pear

Syngenta has submitted magnitude of the residue trials for difenoconazole on apples and pears reflecting currently registered pre-harvest foliar plus proposed post-harvest applications. Five apple trials were conducted during the 2012 growing season in the United States in the North American Free Trade Agreement (NAFTA) Growing Zones 1 (NY, 2 trials), 5 (IL, 1 trial), and 11 (WA and ID, 2 trials). Four pear trials were conducted during the 2012 growing season in the United States in the North American Free Trade Agreement (NAFTA) Growing Zones 10 (CA, 2 trials) and 11 (WA and ID, 2 trials).

Each trial consisted of one treated plot that provided all of the fruit for the post-harvest treatments; there was no untreated plot. At each trial location, the treated plot received five pre-harvest foliar broadcast applications of a 0.73 lb ai/gal emulsion [oil] in water (EW) formulation of difenoconazole (Inspire Super®, Design Code A16001A) at 0.067-0.071 lb ai/A/application for a total seasonal rate of 0.336-0.350 lb ai/A. Applications were made at retreatment intervals (RTIs) of 6-8 days using ground equipment (airblast sprayer) in spray volumes of 98-120 gal/A. A nonionic surfactant (NIS) was added to the spray mixture for each application. Samples of commercially acceptable apples and pears were harvested from all trials at pre-harvest intervals (PHIs) of 14-16 days, except at one CA pear trial (Trial -06) at which fruits were harvested at a 4-day PHI because mature fruits had started falling from the trees. [Note: The product used for the pre-harvest foliar treatments was a multiple active ingredient (MAI) formulation that also contained cyprodinil at 2.09 lb ai/gal; however, data pertaining to cyprodinil are not addressed herein.]

On the day of harvest, samples of pome fruit from each trial were subjected to four different post-harvest treatment techniques with a 2.01 lb ai/gal suspension concentrate (SC) formulation of difenoconazole. The following post-harvest treatments were used: dip for 30 ± 3 seconds at 0.25 lb ai/100 gal water + optional wax (P2); drench for 30 ± 3 seconds at 0.25 lb ai/100 gal water + optional wax (P3); spray with 0.25 lb ai/200,000 lb fruit in sufficient water + required wax/oil (P4); and combined dip + spray, both as above (P5). For treatment P5, fruit was allowed to drain and dry after each treatment and between applications. Application equipment that provided uniform application of the test substance and resulted in adequate coverage of the fruit was used for each treatment type and varied from site to site. Samples were collected after the test substance had dried following post-harvest application. [Note: The product used for the post-harvest treatments was a MAI formulation that also contained fludioxonil at 1.20 lb ai/gal; however data pertaining to fludioxonil are not addressed herein.]

In pome fruits harvested 4 days (one trial) or 14-16 days following five pre-harvest foliar broadcast treatments of a 0.73 lb ai/gal EW formulation of difenoconazole at 0.336-0.350 lb ai/A and subjected to four different post-harvest treatment techniques with a 2.01 lb ai/gal SC formulation, individual sample (and per-trial average) residues in/on apple and pear, respectively, were: 0.584-1.36 ppm (0.594-1.12 ppm) and 0.592-1.06 ppm (0.658-1.06 ppm) following dip treatment for 30 ± 3 seconds at 0.25 lb ai/100 gal water; 0.496-2.61 ppm (0.556-2.59 ppm) and 0.696-1.37 ppm (0.764-1.30 ppm) following drench treatment for 30 ± 3 seconds at 0.25-0.27 lb ai/100 gal water; 0.467-1.41 ppm (0.560-1.39 ppm) and 0.381-1.17 ppm (0.390-1.11 ppm) following spray treatment with 0.24-0.26 lb ai/200,000 lb fruit in water + wax/oil; and

0.924-2.38 ppm (1.12-2.26 ppm) and 0.868-1.62 ppm (0.984-1.61 ppm) following combined dip + spray treatments at the above noted rates.

Table 6. Summary of Residues from Pome Fruit Field Trials with Difenoconazole.

Crop Matrix	Post-Harvest Treatment	Total Application Rate[1]	PTI[2] (days)	n[2]	Residues (ppm)						
					Min.[3]	Max.[3]	LAFT[4]	HAFT[4]	Median[4]	Mean[4]	SD[4]
Apple	Dip (P2)	0.25 lb ai/100 gal	0	5	0.584	1.36	0.594	1.12	0.929	0.917	0.214
	Drench (P3)	0.25-0.27 lb ai/100 gal		5	0.496	2.61	0.556	2.59	1.09	1.25	0.782
	Spray (P4)	0.24-0.26 lb ai/ 200,000 lb fruit		5	0.467	1.41	0.560	1.39	0.632	0.790	0.346
	Dip + Spray (P5)	P2+P4		5	0.924	2.38	1.12	2.26	1.22	1.42	0.477
Pear	Dip (P2)	0.25 lb ai/100 gal	0	4	0.592	1.06	0.658	1.06	0.959	0.909	0.181
	Drench (P3)	0.25-0.27 lb ai/100 gal		4	0.696	1.37	0.764	1.30	0.997	1.01	0.247
	Spray (P4)	0.24-0.25 lb ai/ 200,000 lb fruit		4	0.381	1.17	0.390	1.11	0.629	0.689	0.303
	Dip + Spray (P5)	P2+P4		4	0.868	1.62	0.984	1.61	1.40	1.35	0.276

[1] Total rate reflects post-harvest applications only. However, each trial also received the maximum registered pre-harvest foliar use. At each trial the treated plot received five pre-harvest foliar broadcast treatments at total rates of 0.342-0.350 lb ai/A for apple and 0.336-0.348 lb ai/A for pear with 7-day RTI and 14-day PHI (with one exception; CA pear trial collected at 4-day PHI).
[2] PTI = Post-Treatment Interval n = number of field trials.
[3] Values based on total number of samples.
[4] Values based on per-trial averages. LAFT = lowest average field trial, HAFT = highest average field trial, SD = standard deviation.

Conclusions. The submitted apple and pear magnitude of the residue data were evaluated under a joint review agreement between Health Canada's Pest Management Regulatory Agency (PMRA) and the USEPA. These data are deemed adequate to support the proposed post-harvest uses of difenoconazole on members of pome fruit group 11-10 and reflect the combined currently registered pre-harvest foliar use plus the proposed post-harvest uses. Difenoconazole residue data were collected with an adequate data-collection method and are supported by adequate storage stability data.

Since the maximum residues, highest average residues and recommended tolerances for apple and pear are within 5x, a crop group tolerance can be set for fruit, pome, group 11-10. Using the data reflecting the combined currently registered pre-harvest foliar and proposed dip/drench/spray treatments in the Organization for Economic Cooperation and Development (OECD) tolerance calculation procedures, the recommended tolerance for residues of difenoconazole in/on fruit, pome, group 11-10 is 5.0 ppm. HED notes that while data were generated reflecting a combination of pre-harvest foliar plus post-harvest dip plus spray treatments, the combined post-harvest dip plus spray treatment regimen was not a proposed use in this petition. However, the recommended tolerances would be adequate to cover this particular combined post-harvest use as well.

Although not discussed above, Syngenta also submitted a statistical analysis of the relatively small apple/pear magnitude of the residue dataset using the Mann-Whitney statistical test (submitted via email dated 6/3/14 from T Cox of Syngenta to T. Kish (RD)) in support of their proposed fruit, pome, group 11-10 tolerance (3.0 ppm) determination. *See Appendix III for*

details which will not be discussed further. However, such an analysis is not typically part of the tolerance determination, there is no clear guidance on using statistical analyses for this purpose, and the statistical test generally has low power to detect practical differences between distributions when sample size is small such as in this case. HED have considered the available data/analyses/results and have determined that individual datasets used in the OECD tolerance calculation procedures should not combine different representative crops (i.e., apple/pear) and/or different post-harvest application techniques (i.e., dip/drench/spray/dip+spray). It should be noted that this approach is consistent with current practices. Furthermore, PMRA is expected to use this same approach and revise its MRL in/on members of pome fruit group 11-10 to harmonize with the U.S. recommended tolerance (5.0 ppm) at the end of their review.

860.1520 Processed Food and Feed

Residue Chemistry Memo DP# 340379, 8/9/07, W. Wassell and M. Sahafeyan

Apple

Syngenta previously submitted a processing study for difenoconazole in/on apples. In two trials conducted in NY and WA, five foliar broadcast applications of the 2.1 lb/gal EC formulation were made to apple trees at a target rate of 0.068 lb ai/A/application, for a total seasonal application rate of 0.34 lb ai/A (1x the proposed maximum rate). At each trial, a second plot of apple trees was treated at an exaggerated application rate of 0.34 lb ai/A/application, for a total seasonal rate of 1.7 lb ai/A (5x). Applications were made at RTIs of 7 ± 2 days, and apples were harvested 14 days after the last application. Following harvesting, apples (RAC) were processed into wet pomace and juice using simulated commercial procedures. The average processing factors for apple processed commodities are summarized in Table 7.

Residues of difenoconazole were 0.18 ppm in/on apple RAC samples treated at 1x, and 0.73 and 0.89 ppm in/on apple RAC samples treated at 5x. The processing data indicate that difenoconazole residues do not concentrate in juice (<0.01-0.02 ppm; 0.04x average processing factor) but do concentrate in wet pomace (1.2 and 1.8 ppm in 1x samples, and 6.5 and 11 ppm in 5x samples; 9.5x average processing factor).

Residues of 1,2,4-T were below the LOQ in/on all samples of apple and its processed commodities. Residues of TAA were below the LOQ in/on all samples of apple and its processed commodity, with the exception of one apple juice sample (from apples treated at 5x) which bore quantifiable residues at 0.01 ppm.

Residues of TA were 0.01 and 0.08 ppm in/on apple RAC samples treated at 1x, and 0.02 and 0.19 ppm in/on apple RAC samples treated at 5x. The processing data indicate that TA residues do not concentrate in wet pomace (0.01 and 0.07 ppm in 1x samples, and 0.01 and 0.10 ppm in 5x samples; 0.7x average processing factor) but do concentrate in juice (0.03 and 0.16 ppm in 1x samples, and 0.03 and 0.23 ppm in 5x samples; 1.9x average processing factor).

The reported processing factors do not exceed the theoretical concentration factor for apple pomace of 14x [GLN 860.1520, Table 4; maximum observed (experimental) concentration factor].

Table 7. Summary of Processing Factors for Difenoconazole.					
RAC	Processed Commodity	Average Processing Factor[1]			
		Difenoconazole	1,24-Triazole	Triazole alanine	Triazole acetic acid
Apple	Juice	0.04x	NC	0.7x	NC
	Wet pomace	9.5x	NC	1.9x	NC

[1] NC = Not calculated; residues were below the LOQ in the RAC and the processed commodity.

Conclusions. The previously submitted apple processing data indicate that residues of difenoconazole do not concentrate in juice but do concentrate in wet pomace. Based on the HAFT residues in/on apple (2.59 ppm) and the average processing factor for wet pomace (9.5x), expected residues in wet pomace would be 25 ppm. Because this value is greater than the recommended 5.0 ppm tolerance for fruit, pome, group 11-10, a tolerance is needed for residues of difenoconazole in apple wet pomace at 25 ppm.

860.1650 Submittal of Analytical Reference Standards

Analytical standards for difenoconazole (expiration 11/30/15) and its metabolite CGA-205375 (expiration 8/31/15) are currently available in the EPA National Pesticide Standards Repository.

860.1850 and 860.1900 Confined and Field Accumulation in Rotational Crops

ROCKS Report Memo; DP#391350, 9/19/2011, W. Irwin
Residue Chemistry Memo DP# 382946, 12/7/11, B. Cropp-Kohlligian

The nature of the residue in rotational crops is adequately understood. The metabolism of difenoconazole in rotational crops is similar to that of primary crops. The proposed metabolic pathway for difenoconazole (Company experimental name CGA-169374) involved the degradation of the dioxolane ring to CGA-205374 followed by reduction to CGA-205375. Alternatively, oxidative cleavage of CGA-205374 would lead to CGA-189138.

The HED Residues of Concern Knowledgebase Sub-committee (ROCKS) considered the subject difenoconazole confined rotational crop data and, in consideration of the PBIs indicated by the limited field rotational crop data, determined that only the parent compound needs to be considered as a residue of concern in/on rotational crops at this time (ROCKS Report Memo; DP#391350, 9/19/2011, W. Irwin).

The available difenoconazole confined and limited field rotational crop trials are deemed adequate to satisfy data requirements under Guidelines 860.1850 and 860.1900. Taken together, these data support a 30-day plantback interval (PBI) for cereal and root/tuber crops not already registered for foliar use with difenoconazole and a 60-day PBI for all other crops not already registered for foliar use with difenoconazole.

Note: HED has previously determined, in several reviews, that based on available confined rotational crop data a 30-day PBI for all crops not already registered for use with difenoconazole is appropriate for currently registered/proposed seed treatment uses of difenoconazole. These decisions remain unaltered.

860.1550 Proposed Tolerances

Tolerances for plant commodities are established under §180.475(a)(1), and are expressed in terms of difenoconazole *per se*. The tolerance expression proposed by Syngenta is in terms of difenoconazole *per se*. The tolerances proposed by Syngenta are listed in Table 8, along with the tolerance levels recommended by HED and correct commodity definitions.

The submitted apple and pear magnitude of the residue data were evaluated under a joint review agreement between Health Canada's Pest Management Regulatory Agency (PMRA) and the USEPA. These data are deemed adequate to support the proposed post-harvest uses of difenoconazole on members of pome fruit group 11-10 and reflect the combined currently registered pre-harvest foliar use plus the proposed post-harvest uses. Since the maximum residues, highest average residues and recommended tolerances for apple and pear are within 5x, a crop group tolerance can be set for fruit, pome, group 11-10 and is recommended at 5.0 ppm based on the apple data reflecting the currently registered pre-harvest foliar and the proposed post-harvest drench uses and using the Organization for Economic Cooperation and Development (OECD) tolerance calculation procedures. The recommended tolerance in/on fruit, pome, group 11-10 is not the same as the petitioned-for tolerance increase.

The previously submitted apple processing data indicate that residues of difenoconazole do not concentrate in juice but do concentrate in wet pomace. Based on the HAFT residues in/on apple (2.59 ppm) and the average processing factor for wet pomace (9.5x), the recommended tolerance in apple, wet pomace is 25 ppm. The recommended tolerance in apple, wet pomace is not the same as the petitioned-for tolerance increase.

A Codex maximum residue limit (MRL) for residues of difenoconazole in/on pome fruit is proposed at 0.8 mg/kg based on data reflecting foliar applications of difenoconazole. The Codex MRL would not be adequate to cover residues incurred from the proposed post-harvest uses in the U.S.; therefore, harmonization with Codex is not possible at this time. A Mexican MRL has not been established for the requested crops. A Canadian MRL is established at 1 mg/kg in/on members of pome fruit group 11-10 (listed as individual crops); however, the submitted apple and pear magnitude of the residue data were evaluated under a joint review agreement between Health Canada's Pest Management Regulatory Agency (PMRA) and the USEPA and PMRA is expected to revise its MRL to harmonize with the U.S. recommended tolerance (5.0 ppm) at the end of their review. An International Residue Limit Status Sheet is attached in Appendix I.

Table 8. Tolerance Summary for Difenoconazole.

Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	*Correct Commodity Definition;* Comments
Fruit, pome, group 11-10	3.0	5.0	*Pome fruit group 11-10*
Apple, pomace, wet	7.5	25	*Apple, pomace, wet*

References

DP#s: 172067 and 178394
Subject: PP#2E4051. CGA-169374 (Difenoconazole, Dividend®) in Imported Wheat, Barley, and Rye Grain. First Food Use. CBTS#s 9029, 9895.
From: R. Lascola
To: J. Stone/C. Giles-Parker
Dated: 10/26/92
MRIDs: 42090001-42090004, 42090032-42090059, and 42303901

DP#: 327788
Subject: Triazole-Based Metabolites: Guidance On Residue Chemistry Data Submissions.
From: M. Doherty
To: C. Giles-Parker
Date: 4/25/06
MRIDs: None

DP#: 340379
Subject: PP#6F7115; Difenoconazole. Petition for Establishment of Tolerances on Fruiting Vegetables, Pome Fruit, Sugar Beets, Tuberous and Corm Vegetables, and Imported Papaya. Summary of Analytical Chemistry and Residue Data.
From: W. Wassell/M. Sahafeyan
To: D. Rosenblatt/S. Brothers
Dated: 8/9/07
MRIDs: 46950215-46950237

DP#: None (ACB memo)
Subject: Review of Proposed Tolerance Enforcement Method for Difenoconazole. ACB Project # B07-26.
From: C. Stafford
To: D. Vogel
Dated: 10/29/07
MRIDs: None

DP# 356135
Subject: Difenoconazole. Submission of Residue Analytical Methods Data in Response to DP#265858. Submission of Storage Stability Data in Response to DP#307059. Summary of Analytical Chemistry and Residue Data.
From: B. Cropp-Kohlligian
To: J. Bazuin/T. Kish
Dated: 9/17/09
MRIDs: 47413501 and 47413502

DP#s	361054 and 362648
Subject:	Difenoconazole. Application for Amended Section 3 Registration to Add Uses on Bulb Vegetables, Brassica Leafy Vegetables, Cucurbit Vegetables, Citrus Fruits, Grapes, Pistachios, and Tree Nuts. Submission of Residue Analytical Methods Data in Response to DP#340379. Summary of Analytical Chemistry and Residue Data.
From:	B. Cropp-Kohlligian
To:	R. Kearns/T. Kish
Dated:	9/17/09
MRIDs:	47586101-47586107 and 47648604-47648605

DP#	374898
Subject:	Difenoconazole. The Need for Additional Independent Laboratory Validation (ILV) Information for the Livestock Enforcement Method REM 147.07.
From:	B. Cropp-Kohlligian
To:	R. Kearns/T. Kish
Dated:	3/3/10
MRIDs:	None

DP#	375159
Subject:	Difenoconazole. Dissociation Constant in Water Data to Satisfy OPPTS 830.7370 Guideline Requirements.
From:	B. Cropp-Kohlligian
To:	R. Kearns/T. Kish
Dated:	5/26/10
MRIDs:	47957001

DP#	375194
Subject:	Difenoconazole. Submission of Storage Stability Data in Livestock Commodities in Response to DP# 340379. Submission of a Report of a New Cattle Feeding Study. Summary of Analytical Chemistry and Residue Data.
From:	B. Cropp-Kohlligian
To:	R. Kearns/T. Kish
Dated:	6/17/10
MRIDs:	47957201-47957203

DP#	378829
Subject:	Difenoconazole. Application for Amended Section 3 Registration to Add Uses on Carrots, Chickpeas, Soybeans, Stone Fruits (Group 12), Strawberries, and Turnip Greens. Summary of Analytical Chemistry and Residue Data.
From:	B. Cropp-Kohlligian
To:	R. Kearns/T. Kish
Dated:	2/23/11
MRIDs:	47929801-47929805

DP#: 391350
Subject: Difenoconazole: Report of the Residues of Concern Knowledgebase Sub-committee (ROCKS).
From: W. Irwin, ROCKS Member
Through: C. Olinger and E. Scollon, ROCKS Co-Chairs
To: HED Difenoconazole Risk Assessment Team
Dated: 9/19/11
MRIDs: NA

DP# 382946
Subject: Difenoconazole. Submission of Confined Rotational Crop Data in Response to Data Deficiencies Identified as a Condition of Registration Under Previous Petitions. Summary of Analytical Chemistry and Residue Data.
From: B. Cropp-Kohlligian
To: R. Kearns/T. Kish
Dated: 12/7/11
MRID: 48203402

DP# 363016
Subject: Storage Stability of 1,2,4-Triazole, Triazolylalanine and Triazolylacetic Acid in Various Crop Matrices and Processed Commodities (up to four years under frozen storage).
From: D. Drew
To: T. Gibson
Dated: 1/12/12
MRID: 47606601

DP# 389912
Subject: Difenoconazole. Petition for Post-harvest Use on Tuberous and Corm Vegetables Subgroup 1C and Foliar Uses on Fruiting Vegetables Group 8-10, Citrus Fruits Group 10-10, Pome Fruits Group 11-10, and Low growing Berry Subgroup 13-07G, Except Cranberry. Summary of Analytical Chemistry and Residue Data.
From: B. Cropp-Kohlligian
To: S. Jackson/B. Madden
Dated: 5/30/12
MRID: 48437101

Attachments:
Appendix I. International Residue Limit Status Sheet
Appendix II. Tolerance Assessment Calculations
Appendix III. Syngenta statistical analysis of apple/pear magnitude of the residue data (submitted via email dated 6/3/14 from T Cox of Syngenta to T. Kish (RD) – truncated by reviewer to remove redundancy

Appendix I. International Residue Limit Status Sheet.

Difenoconazole (128847; 7/1/14)

Summary of US and International Tolerances and Maximum Residue Limits			
Residue Definition:			
US	Canada	Mexico[2]	Codex[3]
40 CFR 180.475: Plant: difenoconazole, 1-[2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole Livestock: sum of difenoconazole, 1-[2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole, and its metabolite, CGA-205375, 1-[2-chloro-4-(4-chloro-phenoxy)phenyl]-2-[1,2,4]triazol-1-yl-ethanol, calculated as the stoichiometric equivalent of difenoconazole	1-[2-[4-(4-chlorophenoxy)-2-chlorophenyl]-4-methyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazoledifenoconazole.		Plants: difenoconazole Animal commodities: sum of difenoconazole and 1-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-2-(1,2,4-triazol)-1-yl-ethano), expressed as difenoconazole. The residue is fat-soluble.

Commodity[1]	*Tolerance (ppm) /Maximum Residue Limit (mg/kg)*			
	US	Canada	Mexico[2]	Codex[3]
Fruit, pome, 11-10	5.0	1 apples, Asian pears, azaroles, Chinese quinces, crabapples, Japanese quinces, loquats, mayhaws, medlars, pears, quinces, tejocotes		0.8 pome fruits (proposed)
Apple, wet pomace	25			
Completed: M. Negussie; 07/07/14				

[1] Includes only commodities of interest for this action. Tolerance values should be the HED recommendations and not those proposed by the applicant.

[2] Mexico adopts US tolerances and/or Codex MRLs for its export purposes.

[3] * = absent at the limit of quantitation; Po = postharvest treatment, such as treatment of stored grains. PoP = processed postharvest treated commodity, such as processing of treated stored wheat. (fat) = to be measured on the fat portion of the sample. MRLs indicated as proposed have not been finalized by the CCPR and the CAC.

JMPR Report 2007

Pome fruit
Spanish GAP allows five applications of difenoconazole to apple or pear trees at 0.075 kg ai/ha with a PHI of 14 days. In three trials from Spain, matching GAP, difenoconazole residues in apples were 0.10, 0.14 and 0.15 mg/kg.

In two apple trials from France with application parameters matching Spanish GAP, difenoconazole residues were 0.11 and 0.28 mg/kg.

In two trials from Greece, also with application parameters matching Spanish GAP, difenoconazole residues were 0.05 and 0.13 mg/kg.

In two trials from Italy also with application conditions matching Spanish GAP, difenoconazole residues were 0.06 and 0.08 mg/kg.

In one pear trial from France and one from Greece, matching Spanish GAP, difenoconazole residues in pears were 0.07 and 0.16 mg/kg, respectively.

The Meeting decided to combine the apple and pear data to support a pome fruit MRL.
Residues in the 11 trials in ranked order (median underlined) were: 0.05, 0.06, 0.07, 0.08, 0.10, 0.11, 0.13, 0.14, 0.15, 0.16 and 0.28 mg/kg. The Meeting estimated a maximum residue level, an STMR value and an HR value for difenoconazole in pome fruit of 0.5, 0.11 and 0.28 mg/kg respectively.

Appendix II. Tolerance Assessment Calculations.

The Organization for Economic Cooperation and Development (OECD) tolerance calculation procedures were used for calculating the recommended tolerances. As specified in the OECD document, the average residue from each field trial was used. The rounding procedures specified in the OECD guidelines were also used.

Pome Fruit Group 11-10

The dataset used consisted of apple and pear magnitude of the residue data representing five pre-harvest foliar broadcast treatments of an EW formulation of difenoconazole at 0.07 lb ai/A/application with a 7-day RTI and a 14-day PHI (with one exception) followed by one of the following four different post-harvest treatment techniques: dip for 30 ± 3 seconds at 0.25 lb ai/100 gal water + optional wax (P2); drench for 30 ± 3 seconds at 0.25 lb ai/100 gal water + optional wax (P3); spray with 0.25 lb ai/200,000 lb fruit in sufficient water + required wax/oil (P4); and combined dip + spray, both as above (P5).

The average residues which were used to calculate the tolerance in/on apple and pear are provided below in Tables II-1 and II-2, respectively. Using the Organization for Economic Cooperation and Development (OECD) tolerance calculation procedures, the recommended tolerances are 5.0 ppm in/on apple and 3.0 ppm in/on pear. (See Figures II-1 and II-2) Since the maximum field trial residues, highest average field trial residues and recommended tolerances for apple and pear are within 5x, a crop group tolerance can be set for pome fruit group 11-10 and is recommended at 5.0 ppm based on the apple data reflecting currently registered pre-harvest foliar plus proposed post-harvest drench treatments. The recommended tolerance for residues of difenoconazole in/on pome fruit group 11-10 (5.0 ppm) is not the same as the petitioned-for tolerance (3.0 ppm).

Table II-1. Residue data used to calculate tolerance for difenoconazole post-harvest use in/on apple.	
Regulator:	EPA
Chemical:	Difenoconazole
Crops:	Apple
PHI:	Not Applicable to Post-Harvest Use
App. Rate:	Foliar Treatment: 5 x 0.07 lb ai/A/application; 7-day RTI; 14-day PHI. Plus Post-Harvest Treatment: Dip at 0.25 lb ai/100 gal water + optional wax (P2); Drench at 0.25 lb ai/100 gal water + optional wax (P3); Spray with 0.25 lb ai/200,000 lb fruit in sufficient water + required wax/oil (P4); and combined Dip + Spray, both as above (P5).
Submitter:	Syngenta
MRID Citation:	MRID 49120717

Figure II-1. Tolerance spreadsheet summary of difenoconazole magnitude of the residue data for apple.

Compound	Difenoconazole			
Crop	Apple			
Region/Country	Canada/USA			
GAP	Foliar+Dip (P2)	Foliar+Drench (P3)	Foliar+Spray (P4)	Foliar+Dip+Spray (P5)
Total number of data (n)	5	5	5	5
Percentage of censored data	0%	0%	0%	0%
Number of non-censored data	5	5	5	5
Lowest residue	0.594	0.556	0.560	1.120
Highest residue	1.120	2.590	1.390	2.260
Median residue	0.929	1.090	0.632	1.220
Mean	0.918	1.255	0.790	1.420
Standard deviation (SD)	0.215	0.784	0.346	0.478
Correction factor for censoring (CF)	1.000	1.000	1.000	1.000
Highest residue	1.120	2.590	1.390	2.260
Mean + 4 SD	1.776	4.392	2.175	3.331
CF x 3 mean	2.753	3.766	2.369	4.260
Unrounded MRL	2.753	4.392	2.369	4.260
Rounded MRL	**3**	**5**	**3**	**5**
	High uncertainty of MRL estimate due to small dataset.	High uncertainty of MRL estimate due to small dataset.	High uncertainty of MRL estimate due to small dataset.	High uncertainty of MRL estimate due to small dataset.

	Residues (mg/kg)		Residues (mg/kg)		Residues (mg/kg)		Residues (mg/kg)	
	1.100		1.180		1.390		2.260	
	1.120		2.590		0.632		1.120	
	0.846		1.090		0.560		1.350	
	0.929		0.860		0.586		1.220	
	0.594		0.556		0.780		1.150	

Table II-2. Residue data used to calculate tolerance for difenoconazole post-harvest use in/on pear.	
Regulator:	EPA
Chemical:	Difenoconazole
Crops:	Pear
PHI:	Not Applicable to Post-Harvest Use
App. Rate:	Foliar Treatment: 5 x 0.07 lb ai/A/application; 7-day RTI; 14-day PHI. Plus Post-Harvest Treatment: Dip at 0.25 lb ai/100 gal water + optional wax (P2); Drench at 0.25 lb ai/100 gal water + optional wax (P3); Spray with 0.25 lb ai/200,000 lb fruit in sufficient water + required wax/oil (P4); and combined Dip + Spray, both as above (P5).
Submitter:	Syngenta
MRID Citation:	MRID 49120717

Figure II-2. Tolerance spreadsheet summary of difenoconazole magnitude of the residue data for pear.

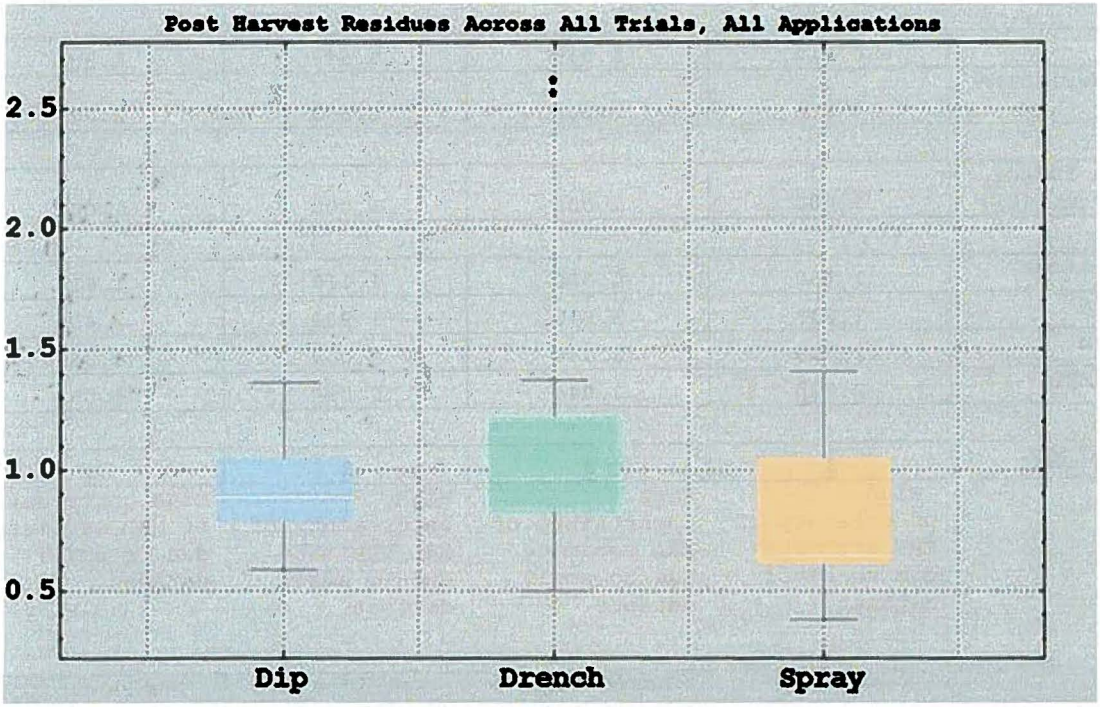
Compound	Difenoconazole			
Crop	Pear			
Region/Country	Canada/USA			
GAP	Foliar+Dip (P2)	Foliar+Drench (P3)	Foliar+Spray (P4)	Foliar+Dip+Spray (P5)
Total number of data (n)	4	4	4	4
Percentage of censored data	0%	0%	0%	0%
Number of non-censored data	4	4	4	4
Lowest residue	0.658	0.764	0.390	0.984
Highest residue	1.060	1.300	1.110	1.610
Median residue	0.960	0.997	0.629	1.405
Mean	0.910	1.015	0.690	1.351
Standard deviation (SD)	0.181	0.249	0.303	0.277
Correction factor for censoring (CF)	1.000	1.000	1.000	1.000
Highest residue	1.060	1.300	1.110	1.610
Mean + 4 SD	1.633	2.010	1.902	2.458
CF x 3 mean	2.729	3.044	2.069	4.053
Unrounded MRL	2.729	3.044	2.069	4.053
Rounded MRL	**3**	**3**	**2**	**4**
	High uncertainty of MRL estimate due to small dataset.	High uncertainty of MRL estimate due to small dataset.	High uncertainty of MRL estimate due to small dataset.	High uncertainty of MRL estimate due to small dataset.

	Residues (mg/kg)		Residues (mg/kg)		Residues (mg/kg)		Residues (mg/kg)	
	1.020		1.300		0.390		1.510	
	1.060		1.140		0.660		1.610	
	0.900		0.854		0.598		0.984	
	0.658		0.764		1.110		1.300	

Appendix III. Syngenta statistical analysis of apple/pear magnitude of the residue data (submitted via email dated 6/3/14 from T Cox of Syngenta to T. Kish (RD) – truncated by reviewer to remove redundancy

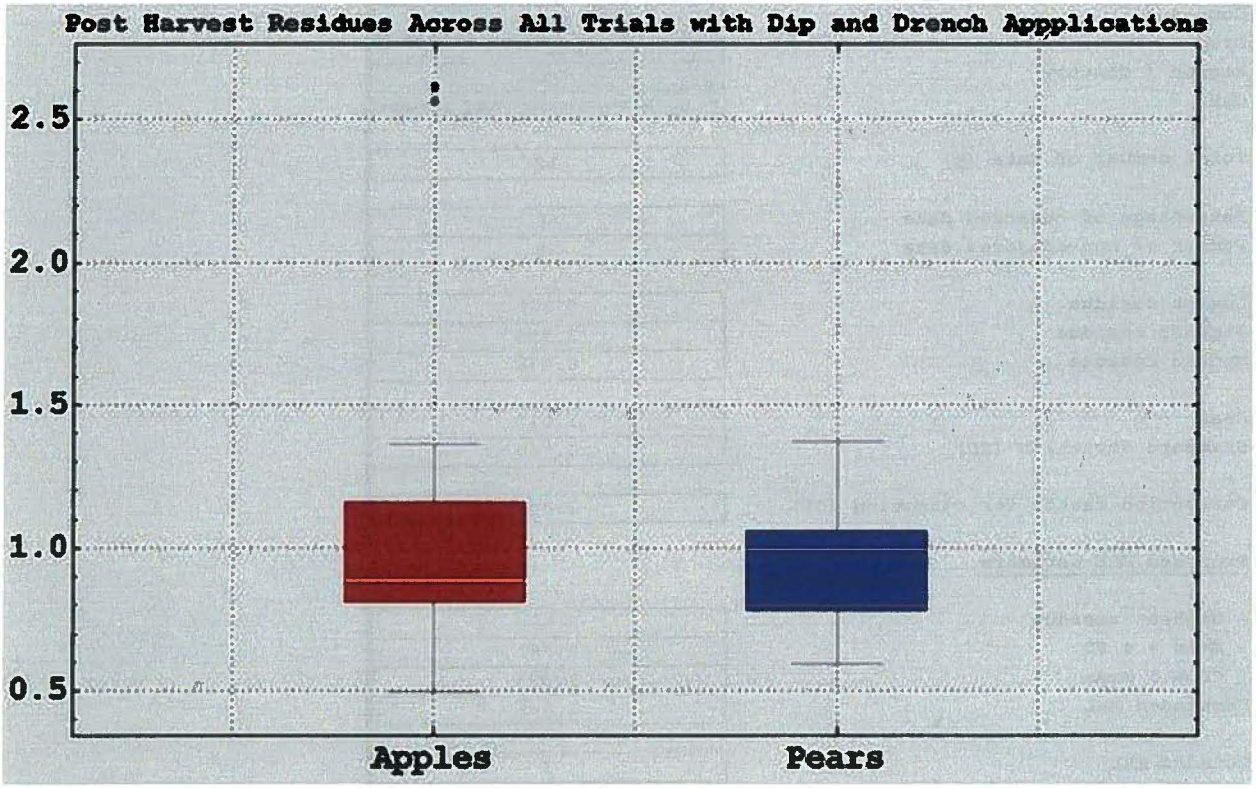
Syngenta submitted a difenoconazole pome fruit residue study with contained data from 9 field trial locations (five in apple and four in pear) where foliar spray applications at the currently registered use rate were followed by post-harvest applications. Three post-harvest application scenarios were employed; dip, drench, and packing line spray.

The data were first subjected to the Mann-Whitney statistical test to assess whether the difference in central tendency (medians) between the two independent populations differs from zero (H0: $\mu 1-\mu 2=0$ versus Ha: $\mu 1-\mu 2\neq 0$). The residue data were grouped by application types (Dip, Drench and Spray). At the $\alpha=0.05$ significance level, and there is no difference between the Dip and Drench application types. However, residues generated from the Drench and Spray applications do not support the assumption that the Drench and Spray application types are the same (i.e., the spray application data are statistically different; lower than from the other two application types).



Based on this statistical analysis Syngenta's position is that the dip and drench residue data should both be utilized in tolerance calculations; whereas the statistically different (and lower) residue data from the spray application should not be used.

Next, to determine if there is any difference between the apple and pear data; the Dip and Drench data sets were grouped by crop (apples and pears). At the $\alpha=0.05$ significance level, the Mann-Whitney test showed that there is no difference between the apple and pear residue dataset. In addition, the whisker diagram below for the combined dataset (dip and drench) shows that the residue distributions are similar. Please note that the apple drench dataset contains the extreme outliers, which were included in these tests.



In addition to the statistical analysis provided above; a comparison of the maximum apple residue (2.59 ppm) and maximum pear residue (1.30 ppm) results in a 2-fold difference, which is well within the 5-fold factor requirement to utilize the data from both crops to support a crop group tolerance per Residue Chemistry Testing Guidelines 860.1500.

Based on these data Syngenta respectfully submits that; 1) the data set for the post-harvest spray application should not be included in the MRL calculation because the data are statistically different (lower) than the data from the post-harvest dip and drench applications, and 2) the apple and pear data are statistically similar and should be combined to provide a more robust data set for use with the MRL calculator. Based on these two data-driven decisions the 18 data points (9 trials x 2 application types) were used in the OECD MRL calculator (see next page).

Compound	Difenoconazole
Crop	Apple/Pear
Region / Country	USA
GAP	Post-Harvest Dip and Drench
Total number of data (n)	18
Percentage of censored data	0%
Number of non-censored data	18
Lowest residue	0.560
Highest residue	2.590
Median residue	0.975
Mean	1.032
Standard deviation (SD)	0.440
Correction factor for censoring (CF)	1.000
Proposed MRL estimate	
- Highest residue	2.590
- Mean + 4 SD	2.793
- CF x 3 Mean	3.095
Unrounded MRL	3.095
Rounded MRL	3

Residues (mg/kg)	
1.100	
1.120	
0.850	
0.930	
0.600	
1.020	
1.060	
0.900	
0.660	
1.180	
2.590	
1.090	
0.860	
0.560	
1.300	
1.140	
0.850	
0.760	

B.7.6 Residues Resulting from Supervised Trials (Annex IIA 6.3; Annex IIIA 8.3)

B.7.6.1 Residues in Target Crops

B.7.6.1.1 Apple and Pear (Fruit, pome, group 11-10)

Document ID: MRID No. 49120717
PMRA No. 2347750

Report: Csinos, A. and Riley, M. (2013) Difenoconazole + Fludioxonil. Inspire Super® (A16001A) and Difenoconazole + Fludioxonil SC (A20171A) – Magnitude of the Residues in or on Apples and Pears as Representative Crops of Pome Fruit, Crop Group 11, USA, 2012. Final Report. Laboratory Project IDs: TK0000656, S12-02340, 69430. Unpublished study prepared by Syngenta Crop Protection, LLC. 267 p.

Guidelines: EPA OCSPP Harmonized Test Guideline 860.1500 Crop Field Trials (August 1996)
PMRA Regulatory Directive DIR98-02 – Residue Chemistry Guidelines, Section 9 – Crop Field Trials
PMRA Regulatory Directive DIR2010-05 – Revisions to the Residue Chemistry Crop Field Trial Requirements
OECD Guideline 509 Crop Field Trial (September 2009)

GLP Compliance: No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

Acceptability: The study is considered scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 417611.

Evaluator: Bonnie Cropp-Kohlligian, Environmental Scientist
Risk Assessment Branch IV (RAB IV)
Health Effects Division (HED) (7509P)

Jianlin Cai, Evaluation Officer
Exposure-1, Health Effects Division I

Note: This Data Evaluation Record (DER) was originally prepared under contract by Versar, Inc. (6850 Versar Center, Springfield, VA 22151; submitted 6/4/14). The DER has been reviewed by HED and revised to reflect current Office of Pesticide Programs (OPP) policies.

EXECUTIVE SUMMARY

Syngenta Crop Protection, LLC has submitted field trials for difenoconazole on apples and pears reflecting pre-harvest plus post-harvest applications. Nine trials were conducted during the 2012 growing season in the United States in the North American Free Trade Agreement (NAFTA) Growing Zones 1 (NY, 2 trials), 5 (IL, 1 trial), and 11 (WA and ID, 2 trials) for apples; and 10 (CA, 2 trials) and 11 (WA and ID, 2 trials) for pears.

Each trial consisted of one treated plot that provided all of the fruit for the post-harvest treatments; there was no untreated plot. At each trial location, the treated plot received five foliar broadcast applications of a 0.73 lb ai/gal (87.5 g ai/L) emulsion [oil] in water (EW) formulation of difenoconazole (Inspire Super®, Design Code A16001A) at 0.067-0.071 lb ai/A/application (75-79.5 g ai/ha/application) for a total seasonal rate of 0.336-0.350 lb ai/A (375-393 g ai/ha). The product was a multiple active ingredient (MAI) formulation that also contained cyprodinil at 2.09 lb ai/gal. Data pertaining to cyprodinil are not addressed herein. Applications were made at retreatment intervals (RTIs) of 6-8 days using ground equipment (airblast sprayer) in spray volumes of 98-120 gal/A (919-1122 L/ha). A nonionic surfactant (NIS) was added to the spray mixture for each application. Samples of commercially acceptable apples and pears were harvested from all trials at pre-harvest intervals (PHIs) of 14-16 days, except at one CA pear trial (Trial -06) at which fruits were harvested at a 4-day PHI because mature fruits had started falling from the trees.

On the day of harvest, samples of pome fruit from each trial were subjected to four different post-harvest treatments with a 2.01 lb ai/gal (240 g ai/L) suspension concentrate (SC) formulation of difenoconazole (Design Code A20171A) which also contained fludioxonil at 1.20 lb ai/gal. Data pertaining to fludioxonil are not addressed herein. The following post-harvest treatments were used: dip for 30 ± 3 seconds at 0.25 lb ai/100 gal (0.30 g ai/L) water + optional wax (P2); drench for 30 ± 3 seconds at 0.25 lb ai/100 gal (0.30 g ai/L) water + optional wax (P3); spray with 0.25 lb ai/200,000 lb fruit (12.5 g ai/10,000 kg fruit) in sufficient water + required wax/oil (P4); and combined dip + spray, both as above (P5). Fruit was allowed to drain and dry after each treatment and between applications for treatment P5. Application equipment that provided uniform application of the test substance and resulted in adequate coverage of the fruit was used for each treatment type and varied from site to site. Samples were collected after the test substance had dried following post-harvest application.

All samples were maintained frozen at the testing facility, during shipping to the laboratory, and were stored frozen until analysis. The maximum storage interval for samples between harvest and extraction for analysis was 155 days (5.1 months). Residues of difenoconazole have been shown to be stable in representative raw agricultural commodities (RACs) for up to 1 year under frozen conditions. Therefore, adequate storage stability data are available to support the storage conditions and intervals for samples in the current trials.

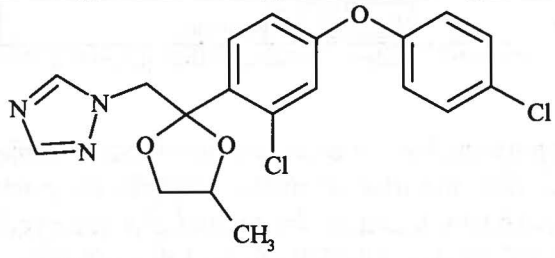
Samples were analyzed for residues of difenoconazole using a high performance liquid chromatography method with tandem mass spectrometry detection (LC-MS/MS), Syngenta Method REM 147.08. Acceptable method validation and concurrent recoveries were reported for pome fruit samples at fortification levels of 0.01-10.0 ppm, thus validating the method. The limit of quantitation (LOQ; determined as the lowest level of method validation, LLMV) was 0.01 ppm.

In pome fruits harvested 4 days (one trial) or 14-16 days following five foliar broadcast applications of a 0.73 lb ai/gal (87.5 g ai/L) EW formulation of difenoconazole at 0.336-0.350 lb ai/A (375-393 g ai/ha) and subjected to four different post-harvest treatments with a 2.01 lb ai/gal (240 g ai/L) SC formulation individual sample (and per-trial average) residues in/on apple and pear, respectively, were: 0.584-1.36 ppm (0.594-1.12 ppm) and 0.592-1.06 ppm (0.658-1.06

ppm) following dip treatment for 30 ± 3 seconds at 0.25 lb ai/100 gal (0.30 g ai/L) water; 0.496-0.261 ppm (0.556-2.59 ppm) and 0.696-1.37 ppm (0.764-1.30 ppm) following drench treatment for 30 ± 3 seconds at 0.25-0.27 lb ai/100 gal (0.30-0.32 g ai/L) water; 0.467-1.41 ppm (0.560-1.39 ppm) and 0.381-1.17 ppm (0.390-1.11 ppm) following spray treatment with 0.24-0.26 lb ai/200,000 lb fruit (12.0-13.0 g ai/10,000 kg fruit) in water + wax/oil; and 0.924-2.38 ppm (1.12-2.26 ppm) and 0.868-1.62 ppm (0.984-1.61 ppm) following combined dip + spray treatments at the above noted rates.

I. MATERIALS AND METHODS

A. MATERIALS

Table B.7.6.1.1-1. Nomenclature for Difenoconazole.	
Common name	Difenoconazole
Identity	1-[[2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-yl]methyl]-1H-1,2,4-triazole
CAS no.	119446-68-3
Company experimental name	CGA-169374
Other synonyms (if applicable)	Not applicable
	

B. Study Design

1. Test Procedure

A total of nine residue trials, five on apples and four on pears, were conducted reflecting pre-harvest foliar applications with a 0.73 lb ai/gal (87.5 g ai/L) EW formulation of difenoconazole followed by four different post-harvest applications with a 2.01 lb ai/gal (240 g ai/L) SC formulation of difenoconazole during the 2012 growing season. The number and locations of the post-harvest trials are adequate based on the following:

- According to DIR98-02 (Section 9) two trials (4 treated samples per trial) are required to support post-harvest uses. Trial locations are not specified for post-harvest uses.
- As per the OECD Guideline for the Testing of Chemicals – Crop Field Trial (9/7/2009), the number of post-harvest trials on a commodity should be at least four, taking into consideration the application techniques, storage facilities, and packing materials used.
- As per the Commission of the European Communities Working Document Guidelines on Comparability, Extrapolation, Group Tolerances and Data Requirements for Setting MRLs (12/6/2001), residues arising from post-harvest treatments are expected to have an inherently higher level of homogeneity and not to be affected by climatic conditions. Differences in residue levels may be associated with different store types and in homogeneous distribution of the applied plant protection product within the stored

products. With regards to the required number of trials, post-harvest treatments were therefore considered as a "single zone worldwide."

All trials, except for those listed in the table below, were separated by >20 miles and are therefore considered independent (568_Criteria for Independence of Trials 04/23/2013; EPA and PMRA). The trials separated by <20 miles have been assessed for independence as detailed in the table below.

Independent Trial Determination[1]			
Crop	Trial Nos.	Differences	Decision
Apple	-01 and -02	Variety: Cortland vs. Granny Smith	Independent due to variety
Pear	-06 and -07	Timing: No off-set in first application, but 4-day PHI in Trial -06 vs. 14-day for Trial -07 because fruits were falling off the tree. Post-harvest adjuvant: Agroschield PD 11620 (wax) vs. none Post-harvest equipment/procedures: Different for all treatment types (dip, drench, spray), conducted on-site by different PFIs Residues: Comparable	Independent due to timing and post-harvest adjuvant and equipment/procedures.

[1] All assessments are based on the replicate trial guidance presented in draft memo 568_Criteria for Independence of Trials 04/23/2013 (EPA and PMRA).

Locations and detailed use patterns for the trials are provided in Table B.7.6.1.1-2. Each trial consisted of one treated plot that provided all of the fruits for the post-harvest treatments; there was no untreated plot. At each trial location, the treated plot received five foliar broadcast applications of a 0.73 lb ai/gal (87.5 g ai/L) EW formulation of difenoconazole. Samples of commercially acceptable apples and pears were harvested from all trials at PHIs of ~14 days, except at one CA pear trial (Trial -06) at which fruit were harvested at a 4-day PHI because mature fruits had started falling from the trees.

On the day of harvest, samples of pome fruit from each trial were subjected to four different post-harvest treatments with a 2.01 lb ai/gal (240 g ai/L) SC formulation of difenoconazole (Design Code A20171A). The following post-harvest treatments were used: dip for 30 ± 3 seconds at 0.25 lb ai/100 gal (0.3 g ai/L) water + optional wax (P2); drench for 30 ± 3 seconds at 0.25 lb ai/100 gal (0.3 g ai/L) water + optional wax (P3); spray with 0.25 lb ai/200,000 lb fruit (12.5 g ai/10,000 kg fruit) in sufficient water + required wax/oil (P4); and combined dip + spray, both as above (P5). Fruits were allowed to drain and dry after each treatment and between applications for treatment P5. Application equipment that provided uniform application of the test substance and resulted in adequate coverage of the fruit was used for each treatment type and varied from site to site. Samples were collected after the test substance had dried following post-harvest application.

Target sample sizes were 24 fruits for each post-harvest treatment. For the dip (P2) treatment, fruits were contained or enclosed in various types of equipment (netting, strainer, mesh bag or wire basket) and completely immersed in the test fungicide solution for approximately 30 seconds, except at Trial -03 where the treatment time was 27-40 seconds. For the drench (P3)

treatment, fruits were placed in a container with holes to allow the solution to drain or on a porous rack or table, and the test solution was slowly poured over the fruit using a watering can or other appropriate equipment for approximately 30 seconds, except at Trial -06 where the appropriate amount of test solution was applied as a drench for a total of 120 seconds. At some trials the fruits were drenched with one-half of the solution, rolled over, and the remainder of the solution was applied. For the spray (P4) treatment, fruits were placed together in blocks or rows on a porous surface. One-half of the test solution was sprayed using a calibrated sprayer to one side of the fruits, the fruits were rolled over, and the remaining solution was sprayed to the underside. For the dip/spray (P5) treatment, a dip application was made following the same procedures described above. The dip treatment was allowed to dry on the fruits and then the fruits were treated with a spray application following the same procedures described above.

Table B.7.6.1.1-2. Study Use Pattern.

Location: City, State; Year (Trial ID)	End-use Product[1]	Method of Application; Timing of Application	Volume[2] (gal/A)	Rate per Application[3] (lb ai/unit)	Retreat-ment Interval[4] (days)	Total Rate[3] (lb ai/unit)	Surfactant/ Adjuvant
Apple							
North Rose, NY; 2012 (TK0000656-01)	0.73 lb ai/gal EW [87.5 g ai/L]	1. Foliar broadcast; BBCH 81, beginning of ripening	99.8 [934 L]	0.068 [76 g ai/ha]	--	0.342 [381 g ai/ha]	NIS
		2. Foliar broadcast; BBCH 81, beginning of ripening	99.6 [931 L]	0.068 [76 g ai/ha]	7		
		3. Foliar broadcast; BBCH 81, beginning of ripening	99.8 [934 L]	0.068 [76 g ai/ha]	6		
		4. Foliar broadcast; BBCH 85, advance of ripening	99.8 [934 L]	0.068 [76 g ai/ha]	7		
		5. Foliar broadcast; BBCH 85, advance of ripening	100.2 [937 L]	0.068 [76 g ai/ha]	8		
	2.01 lb ai/gal SC [240 g ai/L]	P2. Post-harvest dip; BBCH 87	71 mL EP/15 gal	0.25 [0.30 g ai/L]	14	0.25 [0.30 g ai/L]	None
		P3. Post-harvest drench; BBCH 87	23.7 mL EP/5 gal	0.25 [0.30 g ai/L]	14	0.25 [0.30 g ai/L]	None
		P4. Post-harvest spray; BBCH 87	8.4 mL EP/1 L	0.25 [12.5 g ai/unit]	14	0.25 [12.5 g ai/unit]	Carnuba wax
		P5. Post-harvest dip + spray; BBCH 87	P2 + P4	P2 + P4	14	P2 + P4	None/Car-nuba wax

Table B.7.6.1.1-2. Study Use Pattern.

Location: City, State; Year (Trial ID)	End-use Product[1]	Method of Application; Timing of Application	Volume[2] (gal/A)	Rate per Application[3] (lb ai/unit)	Retreat-ment Interval[4] (days)	Total Rate[3] (lb ai/unit)	Surfactant/ Adjuvant
Alton, NY; 2012 (TK0000656-02)	0.73 lb ai/gal EW [87.5 g ai/L]	1. Foliar broadcast; BBCH 76, fruit 60% final size	100.4 [939 L]	0.068 [76 g ai/ha]	--	0.342 [381 g ai/ha]	NIS
		2. Foliar broadcast; BBCH 77, fruit 70% final size	100.0 [935 L]	0.068 [76 g ai/ha]	7		
		3. Foliar broadcast; BBCH 77, fruit 70% final size	100.2 [937 L]	0.068 [76 g ai/ha]	7		
		4. Foliar broadcast; BBCH 77, fruit 70% final size	100.2 [937 L]	0.068 [76 g ai/ha]	7		
		5. Foliar broadcast; BBCH 78, fruit 80% final size	100.0 [935 L]	0.068 [76 g ai/ha]	7		
	2.01 lb ai/gal SC [240 g ai/L]	P2. Post-harvest dip; BBCH 87	23.7 mL EP/5 gal	0.25 [0.30 g ai/L]	16	0.25 [0.30 g ai/L]	None
		P3. Post-harvest drench; BBCH 87	23.7 mL EP/5 gal	0.25 [0.30 g ai/L]	16	0.25 [0.30 g ai/L]	None
		P4. Post-harvest spray; BBCH 87	0.7 mL EP/1 L	0.25 [12.5 g ai/unit]	16	0.25 [12.5 g ai/unit]	Carnuba wax
		P5. Post-harvest dip + spray; BBCH 87	P2 + P4	P2 + P4	16	P2 + P4	None + Car-nuba wax
Marengo, IL; 2012 (TK0000656-03)	0.73 lb ai/gal EW [87.5 g ai/L]	1. Foliar broadcast; 2" diameter	117.9 [1103 L]	0.068 [76 g ai/ha]	--	0.343 [383 g ai/ha]	NIS
		2. Foliar broadcast; 3-4" diameter	117.5 [1099 L]	0.068 [76 g ai/ha]	7		
		3. Foliar broadcast; 4" diameter	119.7 [1120 L]	0.068 [76 g ai/ha]	7		
		4. Foliar broadcast; 4" diameter	120.0 [1122 L]	0.069 [77 g ai/ha]	8		
		5. Foliar broadcast; 4" diameter, turning red	119.9 [1122 L]	0.069 [77 g ai/ha]	6		
	2.01 lb ai/gal SC [240 g ai/L]	P2. Post-harvest dip; BBCH 89	99.5 mL EP/21 gal	0.25 [0.30 g ai/L]	15	0.25 [0.30 g ai/L]	None
		P3. Post-harvest drench; BBCH 89	99.5 mL EP/21 gal	0.25 [0.30 g ai/L]	15	0.25 [0.30 g ai/L]	None
		P4. Post-harvest spray; BBCH 89	0.9 mL EP/140.8 mL	0.26 [13.0 g ai/unit]	15	0.26 [13.0 g ai/unit]	Prima Fresh Ultra
		P5. Post-harvest dip + spray; BBCH 89	P2 + P4	P2 + P4	15	P2 + P4	None + Prime Fresh Ultra
Ephrata, WA; 2012 (TK0000656-04)	0.73 lb ai/gal EW [87.5 g ai/L]	1. Foliar broadcast; BBCH 80	100.5	0.070 [78 g ai/ha]	--	0.350 [393 g ai/ha]	NIS
		2. Foliar broadcast; BBCH 81	100.5 [940 L]	0.070 [78 g ai/ha]	7		
		3. Foliar broadcast; BBCH 82	100.5 [940 L]	0.070 [78 g ai/ha]	7		
		4. Foliar broadcast; BBCH 83	101.3 [948 L]	0.070 [78 g ai/ha]	7		

Table B.7.6.1.1-2. Study Use Pattern.

Location: City, State; Year (Trial ID)	End-use Product[1]	Method of Application; Timing of Application	Volume[2] (gal/A)	Rate per Application[3] (lb ai/unit)	Retreat-ment Interval[4] (days)	Total Rate[3] (lb ai/unit)	Surfactant/ Adjuvant
		5. Foliar broadcast; BBCH 86	101.6 [950 L]	0.071 [80 g ai/ha]	7		
	2.01 lb ai/gal SC [240 g ai/L]	P2. Post-harvest dip; BBCH 89	43.0 mL EP/9.1 gal	0.25 [0.30 g ai/L]	14	0.25 [0.30 g ai/L]	None
		P3. Post-harvest drench; BBCH 89	24.0 mL EP/5 gal	0.25 [0.30 g ai/L]	14	0.25 [0.30 g ai/L]	None
		P4. Post-harvest spray; BBCH 89	1.0 mL EP/165 mL	0.24 [12.0 g ai/unit]	14	0.24 [12.0 g ai/unit]	Phase 3 Golden
		P5. Post-harvest dip + spray; BBCH 89	P2 + P4	P2 + P4	14	P2 + P4	None + Phase 3 Golden
Weiser, ID; 2012 (TK0000656-05)	0.73 lb ai/gal EW [87.5 g ai/L]	1. Foliar broadcast; BBCH 78, fruit 80% final size	103.1 [964 L]	0.071 [80 g ai/ha]	--	0.347 [390 g ai/ha]	NIS
		2. Foliar broadcast; BBCH 78, fruit 80% final size	101.4 [948 L]	0.070 [78 g ai/ha]	7		
		3. Foliar broadcast; BBCH 78, fruit 80% final size	101.6 [950 L]	0.070 [78 g ai/ha]	7		
		4. Foliar broadcast; BBCH 79, fruit 90% final size	100.4 [939 L]	0.069 [77 g ai/ha]	6		
		5. Foliar broadcast; BBCH 85, fruit with advanced coloring	100.1 [936 L]	0.068 [76 g ai/ha]	7		
	2.01 lb ai/gal SC [240 g ai/L]	P2. Post-harvest dip; BBCH 89	18.8 mL EP/3.96 gal	0.25 [0.30 g ai/L]	14	0.25 [0.30 g ai/L]	None
		P3. Post-harvest drench; BBCH 89	2.50 mL EP/0.5 gal	0.27 [0.32 g ai/L]	14	0.27 [0.32 g ai/L]	None
		P4. Post-harvest spray; BBCH 89	2.0 mL EP/240 mL	0.25 [12.5 g ai/unit]	14	0.25 [12.5 g ai/unit]	Phase 3 Carnauba Plus
		P5. Post-harvest dip + spray; BBCH 89	P2 + P4	P2 + P4	14	P2 + P4	None + Phase 3 Carnuba Plus
Pear							
Madera, CA; 2012 (TK0000656-06)	0.73 lb ai/gal EW [87.5 g ai/L]	1. Foliar broadcast; 2" diameter	99.9 [934 L]	0.067 [75 g ai/ha]	--	0.336 [375 g ai/ha]	NIS
		2. Foliar broadcast; 2-2.25" diameter	98.9 [925 L]	0.067 [75 g ai/ha]	7		
		3. Foliar broadcast; 3-4" diameter	99.9 [934 L]	0.067 [75 g ai/ha]	7		
		4. Foliar broadcast; 3-5" diameter	99.8 [934 L]	0.067 [75 g ai/ha]	7		
		5. Foliar broadcast; fruit full size, almost ready to harvest	100.2 [937 L]	0.067 [75 g ai/ha]	7		
	2.01 lb ai/gal SC [240	P2. Post-harvest dip; BBCH 87	38 mL EP/8 gal	0.25 [0.30 g ai/L]	4	0.25 [0.30 g ai/L]	AgroSchield PD 1620

Table B.7.6.1.1-2. Study Use Pattern.

Location: City, State; Year (Trial ID)	End-use Product[1]	Method of Application; Timing of Application	Volume[2] (gal/A)	Rate per Application[3] (lb ai/unit)	Retreat-ment Interval[4] (days)	Total Rate[3] (lb ai/unit)	Surfactant/ Adjuvant
	g ai/L]	P3. Post-harvest drench; BBCH 87	9.5 mL EP/2 gal	0.25 [0.30 g ai/L]	4	0.25 [0.30 g ai/L]	AgroSchield PD 1620
		P4. Post-harvest spray; BBCH 87	12.5 mL EP/2 L	0.25 [12.5 g ai/unit]	4	0.25 [12.5 g ai/unit]	AgroSchield PD 1620
		P5. Post-harvest dip + spray; BBCH 87	P2 + P4	P2 + P4	4	P2 + P4	AgroSchield PD 1620
Madera, CA; 2012 (TK0000656-07)	0.73 lb ai/gal EW [87.5 g ai/L]	1. Foliar broadcast; BBCH 77	99.9 [934 L]	0.069 [77 g ai/ha]	--	0.346 [388 g ai/ha]	NIS
		2. Foliar broadcast; BBCH 78	98.2 [919 L]	0.068 [75 g ai/ha]	7		
		3. Foliar broadcast; BBCH 79	100.5 [940 L]	0.070 [78 g ai/ha]	7		
		4. Foliar broadcast; BBCH 81	101.7 [951 L]	0.070 [78 g ai/ha]	7		
		5. Foliar broadcast; BBCH 85	100.0 [935 L]	0.069 [76 g ai/ha]	7		
	2.01 lb ai/gal SC [240 g ai/L]	P2. Post-harvest dip; BBCH 89	47 mL EP/10 gal	0.25 [0.30 g ai/L]	14	0.25 [0.30 g ai/L]	None
		P3. Post-harvest drench[5]; BBCH 89	3.70 mL EP/0.8 gal	0.25 [0.30 g ai/L]	14	0.25 [0.30 g ai/L]	None
		P4. Post-harvest spray; BBCH 89	0.42 mL EP/50 mL	0.25 [12.5 g ai/unit]	14	0.25 [12.5 g ai/unit]	None
		P5. Post-harvest dip + spray; BBCH 89	P2 + P4	P2 + P4	14	P2 + P4	None
Ephrata, WA; 2012 (TK0000656-08)	0.73 lb ai/gal EW [87.5 g ai/L]	1. Foliar broadcast; BBCH 81	100.8 [943 L]	0.070 [78 g ai/ha]	--	0.348 [392 g ai/ha]	NIS
		2. Foliar broadcast; BBCH 82	100.1 [936 L]	0.070 [78 g ai/ha]	7		
		3. Foliar broadcast; BBCH 83	100.1 [936 L]	0.070 [78 g ai/ha]	7		
		4. Foliar broadcast; BBCH 84	100.6 [941 L]	0.070 [78 g ai/ha]	7		
		5. Foliar broadcast; BBCH 86	100.6 [941 L]	0.070 [78 g ai/ha]	7		
	2.01 lb ai/gal SC [240 g ai/L]	P2. Post-harvest dip; BBCH 89	43 mL EP/9.1 gal	0.25 [0.30 g ai/L]	14	0.25 [0.30 g ai/L]	None
		P3. Post-harvest drench; BBCH 89	24.0 mL EP/5 gal	0.25 [0.30 g ai/L]	14	0.25 [0.30 g ai/L]	None
		P4. Post-harvest spray; BBCH 89	1.0 mL EP/165 mL	0.24 [12.0 g ai/unit]	14	0.24 [12.0 g ai/unit]	Phase 3 Golden
		P5. Post-harvest dip + spray; BBCH 89	P2 + P4	P2 + P4	14	P2 + P4	None + Phase 3 Golden

Table B.7.6.1.1-2. Study Use Pattern.

Location: City, State; Year (Trial ID)	End-use Product[1]	Method of Application; Timing of Application	Volume[2] (gal/A)	Rate per Application[3] (lb ai/unit)	Retreat-ment Interval[4] (days)	Total Rate[3] (lb ai/unit)	Surfactant/ Adjuvant
Payette, ID; 2012 (TK0000656-09)	0.73 lb ai/gal EW [87.5 g ai/L]	1. Foliar broadcast; BBCH 89	102.7 [961 L]	0.071 [80 g ai/ha]	--	0.349 [392 g ai/ha]	NIS
		2. Foliar broadcast; BBCH 76-77, fruit 60-79% final size	100.8 [943 L]	0.070 [78 g ai/ha]	7		
		3. Foliar broadcast; BBCH 77-78, fruit 70-80% final size	101.1 [946 L]	0.070 [78 g ai/ha]	7		
		4. Foliar broadcast; BBCH 78-79	99.7 [933 L]	0.068 [76 g ai/ha]	7		
		5. Foliar broadcast; BBCH 79, fruit 90% final size	102.8 [962 L]	0.071 [80 g ai/ha]	7		
	2.01 lb ai/gal SC [240 g ai/L]	P2. Post-harvest dip; BBCH 87	18.8 mL EP/4.0 gal	0.25 [0.30 g ai/L]	14	0.25 [0.30 g ai/L]	None
		P3. Post-harvest drench; BBCH 87	2.5 mL EP/0.5 gal	0.27 [0.32 g ai/L]	14	0.27 [0.32 g ai/L]	None
		P4. Post-harvest spray; BBCH 87	6.8 mL EP/1 L	0.25 [12.5 g ai/unit]	14	0.25 [12.5 g ai/unit]	Phase 3 Carnauba Plus
		P5. Post-harvest dip + spray; BBCH 87	P2 + P4	P2 + P4	14	P2 + P4	None + Phase 3 Carnuba Plus

[1] For pre-harvest applications: 0.73 lb ai/gal (87.5 g ai/L) EW formulation of difenoconazole (Inspire Super®, Design Code A16001A; MAI containing cyprodinil at 2.09 lb ai/gal). For post-harvest applications: 2.01 lb ai/gal (240 g ai/L) SC formulation of difenoconazole (Design Code A20171A; MAI containing fludioxonil at 1.20 lb ai/gal).
[2] gal/A except as noted for post-harvest applications.
[3] Rate in lb ai/A for foliar applications, lb ai/100 gal for post-harvest dip and drench applications, and lb ai/200,000 lb fruit [g ai/10,000 kg fruit] for post-harvest spray applications. Total application rate reflects the sum of foliar applications for pre-harvest applications and individual application rate for each post-harvest treatment.
[4] The retreatment interval for post-harvest applications corresponds to the PHI.
[5] The petitioner reported that the post-harvest drench application at this trial (-07) was made with a CO_2 backpack sprayer with a single nozzle rather than poured over the sample.

Crops were grown and maintained according to typical agricultural practices. Irrigation was used at most trial sites. No unusual weather conditions were reported to have adversely affected crop growth or yield during the study; however, the petitioner noted that due to cold weather conditions, one trial (Trial -02) was conducted in a location that had been treated with conazole type fungicides the previous season.

Sample Handling and Preparation

Samples were placed in frozen storage at the field sites after post-harvest applications as soon as the test solution had dried. All samples were shipped within 32 days of collection to the analytical laboratory, Morse Laboratories (Sacramento, CA) for residue analysis. The samples were stored frozen (<-10 °C) at the analytical laboratory prior to homogenization in the presence of dry ice and analysis. Samples of untreated apples and pears were purchased locally for use in method validation and concurrent recovery analyses.

2. Description of Analytical Procedures

Samples were analyzed for residues of difenoconazole using an LC-MS/MS method, Syngenta Method REM 147.08 (modifications dated 10/17/08). This method was previously used for data collection in the field rotational crop study reviewed under DP# 340379 (8/9/07, W. Wassell) [PMRA# 1856763]. A brief description of the method was included in the submission.

Briefly, samples were extracted with methanol:concentrated ammonium hydroxide (80:20, v:v) via heating at reflux for 2 hours. An aliquot of the extract was diluted with water and cleaned up by solid phase extraction (SPE) on an Oasis™ HLB cartridge. Residues were eluted with dichloromethane:ethyl acetate (80:20, v:v). The eluate was evaporated to dryness and redissolved in ACN:water (1:1, v:v) for LC-MS/MS analysis. The LOQ was 0.01 ppm. The LOD was not provided.

II. RESULTS AND DISCUSSION

Method performance was evaluated during method validation and by use of concurrent recovery samples. For method validation, three samples each of untreated pear were fortified at 0.01 and 10.0 ppm; individual recoveries were 86-96% with a standard deviation of <2.3% for both levels. For concurrent recovery, twelve samples of apple were fortified at 0.01, 1.0, and 3.0 ppm (n = 6, 5, and 1), and individual recoveries (and standard deviations), respectively, were 99-108% (3.1%), 97-102% (2.1%), and 106% (not applicable). Ten samples of pear were fortified at 0.01, 1.0, and 2.0 ppm (n = 5, 4, and 1), and individual recoveries (and standard deviations), respectively, were 100-110% (4.0%), 97-109% (5.2%), and 106% (not applicable). All recoveries were within the acceptable range of 70%-120%; therefore, the method was considered valid for the analysis of difenoconazole residues in pome fruit matrices. The fortification levels bracketed the measured residues. Concurrent recoveries were corrected for apparent residues in controls (purchased samples).

The detector response was linear (coefficient of determination, r^2 >0.999) within the range of 0.000125-0.005 µg/mL. Representative chromatograms of control samples, fortified samples and treated samples were provided. The control chromatograms generally had no peaks of interest above the chromatographic background. The fortified sample chromatograms contained only the analyte of interest, and peaks were symmetrical and well defined. Residues in controls (purchased samples) were <0.01 ppm. The reported residue values were not corrected for apparent residues in controls.

The field residue samples were stored frozen a maximum of 155 days (5.1 months) from harvest to analysis (Table B.7.6.1.1-3). Acceptable storage stability data are available indicating that residues of difenoconazole were stable in raw agricultural crop commodities (RACs) for up to 1 year when stored under frozen conditions.

Table B.7.6.1.1-3. Summary of Storage Conditions.			
Matrix (RAC or Extract)	Storage Temperature (°C)	Actual Storage Duration[1]	Interval of Demonstrated Storage Stability
Apple and pear	<-10	119-155 days (3.9-5.1 months)	Residues of difenoconazole were stable in RACs for up to 1 year when stored under frozen conditions.[2]

[1] Interval from harvest to extraction. Samples were analyzed within 0-4 days of extraction.
[2] DP# 356135, 9/17/09, B. Cropp-Kohlligian; REG2006-08

The results from the submitted field trials are presented in Tables B.7.6.1.1-4 and B.7.6.1.1-5. In pome fruits harvested 4 days (one trial) or 14-16 days following five foliar broadcast applications of a 0.73 lb ai/gal (87.5 g ai/L) EW formulation of difenoconazole at a total rate of 0.336-0.350 lb ai/A (375-393 g ai/ha) and subjected to four different post-harvest treatments with a 2.01 lb ai/gal (240 g ai/L) SC formulation individual sample (and per-trial average) residues in/on apples and pears, respectively, were: 0.584-1.36 ppm (0.594-1.12 ppm) and 0.592-1.06 ppm (0.658-1.06 ppm) following dip treatment for 30 ± 3 seconds at 0.25 lb ai/100 gal (0.30 g ai/L) water; 0.496-0.261 ppm (0.556-2.59 ppm) and 0.696-1.37 ppm (0.764-1.30 ppm) following drench treatment for 30 ± 3 seconds at 0.25-0.27 lb ai/100 gal (0.30-0.32 g ai/L) water; 0.467-1.41 ppm (0.560-1.39 ppm) and 0.381-1.17 ppm (0.390-1.11 ppm) following spray treatment with 0.24-0.26 lb ai/200,000 lb fruit (12.0-13.0 g ai/10,000 kg fruit) in water + wax/oil; and 0.924-2.38 ppm (1.12-2.26 ppm) and 0.868-1.62 ppm (0.984-1.61 ppm) following combined dip + spray treatments at the above noted rates.

Table B.7.6.1.1-4. Residue Data from Pome Fruit Field Trials with Difenoconazole.[1]

Location: City, State Year (Trial ID)	Zone	Variety	Matrix	Post-Harvest Treatment[2]	Rate (lb ai/unit)[3]		PHI/ PTI[4] (days)	Residues[5] (ppm [Average]
					Foliar	Post-Harvest		
Apple								
North Rose, NY; 2012 (TK0000656-01)	1	Cortland	Fruit	Dip (P2)	0.342 [381 g ai/ha]	0.25 [0.30 g ai/L]	14/0	1.03, 1.16 [1.10]
				Drench (P3)		0.25 [0.30 g ai/L]		1.23, 1.12 [1.18]
				Spray (P4)		0.25 [12.5 g ai/unit]		1.37, 1.41 [1.39]
				Dip + Spray (P5)		P2 + P4		2.38, 2.13 [2.26]
Alton, NY; 2012 (TK0000656-02)	1	Granny Smith	Fruit	Dip (P2)	0.342 [381 g ai/ha]	0.25 [0.30 g ai/L]	16/0	1.36, 0.880 [1.12]
				Drench (P3)		0.25 [0.30 g ai/L]		2.61, 2.56 [2.59]
				Spray (P4)		0.25 [12.5 g ai/unit]		0.644, 0.620 [0.632]
				Dip + Spray (P5)		P2 + P4		1.31, 0.924 [1.12]

Table B.7.6.1.1-4. Residue Data from Pome Fruit Field Trials with Difenoconazole.[1]

Location: City, State Year (Trial ID)	Zone	Variety	Matrix	Post-Harvest Treatment[2]	Rate (lb ai/unit)[3]		PHI/ PTI[4] (days)	Residues[5] (ppm [Average]
					Foliar	Post-Harvest		
Marengo, IL; 2012 (TK0000656-03)	5	Red Chief	Fruit	Dip (P2)	0.343 [383 g ai/ha]	0.25 [0.30 g ai/L]	15/0	0.884, 0.808 [0.846]
				Drench (P3)		0.25 [0.30 g ai/L]		1.21, 0.964 [1.09]
				Spray (P4)		0.26 [13.0 g ai/unit]		0.608, 0.512 [0.560]
				Dip + Spray (P5)		P2 + P4		1.39, 1.31 [1.35]
Ephrata, WA; 2012 (TK0000656-04)	11	Red Delicious	Fruit	Dip (P2)	0.350 [393 g ai/ha]	0.25 [0.30 g ai/L]	14/0	0.808, 1.05 [0.929]
				Drench (P3)		0.25 [0.30 g ai/L]		0.840, 0.880 [0.860]
				Spray (P4)		0.24 [12.0 g ai/unit]		0.467, 0.704 [0.586]
				Dip + Spray (P5)		P2 + P4		1.16, 1.28 [1.22]
Weiser, ID; 2012 (TK0000656-05)	11	Early Spur Rome	Fruit	Dip (P2)	0.347 [390 g ai/ha]	0.25 [0.30 g ai/L]	14/0	0.584, 0.604 [0.594]
				Drench (P3)		0.27 [0.32 g ai/L]		0.616, 0.496 [0.556]
				Spray (P4)		0.25 [12.5 g ai/unit]		0.724, 0.836 [0.780]
				Dip + Spray (P5)		P2 + P4		1.08, 1.21 [1.15]
Pear								
Madera, CA; 2012 (TK0000656-06)	10	Asian	Fruit	Dip (P2)	0.336 [375 g ai/ha]	0.25 [0.30 g ai/L]	4/0	1.04, 0.996 [1.02]
				Drench (P3)		0.25 [0.30 g ai/L]		1.37, 1.22 [1.30]
				Spray (P4)		0.25 [12.5 g ai/unit]		0.398, 0.381 [0.390]
				Dip + Spray (P5)		P2 + P4		1.45, 1.56 [1.51]
Madera, CA; 2012 (TK0000656-07)	10	Asian, Ho Sai	Fruit	Dip (P2)	0.346 [388 g ai/ha]	0.25 [0.30 g ai/L]	14/0	1.06, 1.06 [1.06]
				Drench (P3)		0.25 [0.30 g ai/L]		1.11, 1.17 [1.14]
				Spray (P4)		0.25 [12.5 g ai/unit]		0.712, 0.608 [0.660]
				Dip + Spray (P5)		P2 + P4		1.60, 1.62 [1.61]
Ephrata, WA; 2012 (TK0000656-08)	11	Concorde	Fruit	Dip (P2)	0.348 [392 g ai/ha]	0.25 [0.30 g ai/L]	14/0	1.02, 0.780 [0.900]
				Drench (P3)		0.25 [0.30 g ai/L]		0.816, 0.892 [0.854]
				Spray (P4)		0.24 [12.0 g ai/unit]		0.612, 0.584 [0.598]
				Dip + Spray (P5)		P2 + P4		0.868, 1.10 [0.984]
Payette, ID; 2012	11	Bartlett	Fruit	Dip (P2)	0.349 [392 g ai/ha]	0.25 [0.30 g ai/L]	14/0	0.724, 0.592 [0.658]
				Drench (P3)		0.27		0.832, 0.696 [0.764]

Table B.7.6.1.1-4. Residue Data from Pome Fruit Field Trials with Difenoconazole.[1]

Location: City, State Year (Trial ID)	Zone	Variety	Matrix	Post-Harvest Treatment[2]	Rate (lb ai/unit)[3]		PHI/ PTI[4] (days)	Residues[5] (ppm [Average]
					Foliar	Post-Harvest		
(TK0000656-09)						[0.32 g ai/L]		
				Spray (P4)		0.25 [12.5 g ai/unit]		1.17, 1.05 [1.11]
				Dip + Spray (P5)		P2 + P4		1.30, 1.30 [1.30]

[1] End-use products: for pre-harvest applications: 0.73 lb ai/gal (87.5 g ai/L) EW formulation of difenoconazole (Inspire Super®, Design Code A16001A; MAI containing cyprodinil at 2.09 lb ai/gal); for post-harvest applications: 2.01 lb ai/gal (240 g ai/L) SC formulation of difenoconazole (Design Code A20171A; MAI containing fludioxonil at 1.20 lb ai/gal).
[2] At each trial the treated plot received five foliar broadcast applications. On the day of harvest, samples of pome fruit from each trial were subjected to four different post-harvest treatments, including: dip for 30 ± 3 seconds at 0.25 lb ai/100 gal water + optional wax (P2); drench for 30 ± 3 seconds at 0.25 lb ai/100 gal water + optional wax (P3); spray with 0.25 lb ai/200,000 lb fruit [g ai/10,000 kg fruit] in sufficient water + required wax/oil (P4); and combined dip + spray, both as above (P5).
[3] Rate in lb ai/A for foliar applications, lb ai/100 gal for post-harvest dip and drench applications, and lb ai/200,000 lb fruit for post-harvest spray applications.
[4] PTI = Post-treatment interval. Post-harvest applications were made on the day of harvest.
[5] The LOQ was 0.01 ppm. Per-trial averages were calculated by the study reviewer.

Table B.7.6.1.1-5. Summary of Residues from Pome Fruit Field Trials with Difenoconazole.

Crop Matrix	Post-Harvest Treatment	Total Application Rate[1] (lb ai/unit)	PTI (days)	n[2]	Residues (ppm)						
					Min.[3]	Max.[3]	LAFT[4]	HAFT[4]	Median[4]	Mean[4]	SD[4]
Apple	Dip (P2)	0.25 [0.30 g ai/L]	0	5	0.584	1.36	0.594	1.12	0.929	0.917	0.214
	Drench (P3)	0.25-0.27 [0.30-0.32 g ai/L]		5	0.496	2.61	0.556	2.59	1.09	1.25	0.782
	Spray (P4)	0.24-0.26 [12.0-13.0 g ai/ 10,000 kg fruit]		5	0.467	1.41	0.560	1.39	0.632	0.790	0.346
	Dip + Spray (P5)	P2+P4		5	0.924	2.38	1.12	2.26	1.22	1.42	0.477
Pear	Dip (P2)	0.25 [0.30 g ai/L]	0	4	0.592	1.06	0.658	1.06	0.959	0.909	0.181
	Drench (P3)	0.25-0.27 [0.30-0.32 g ai/L]		4	0.696	1.37	0.764	1.30	0.997	1.01	0.247
	Spray (P4)	0.24-0.25 [12.0-13.0 g ai/ 10,000 kg fruit]		4	0.381	1.17	0.390	1.11	0.629	0.689	0.303
	Dip + Spray (P5)	P2+P4		4	0.868	1.62	0.984	1.61	1.40	1.35	0.276

[1] Rate in lb ai/100 gal for post-harvest dip and drench applications and lb ai/200,000 lb apples for post-harvest spray applications. Total rate reflects post-harvest applications only. At each trial the treated plot received five foliar broadcast applications at total rates of 0.342-0.350 lb ai/A (383-393 g ai/ha) for apple and 0.336-0.348 lb ai/A (375-390 g ai/ha) for pear.
[2] n = number of field trials.
[3] Values based on total number of samples.
[4] Values based on per-trial averages. LAFT = lowest average field trial, HAFT = highest average field trial, SD = standard deviation.

III. CONCLUSIONS

The pome fruit field trials are considered scientifically acceptable. The results of the study showed that in pome fruits harvested 4 days (one trial) or 14-16 days following five foliar broadcast applications of a 0.73 lb ai/gal (87.5 g ai/L) EW formulation of difenoconazole at a total rate of 0.336-0.350 lb ai/A (375-393 g ai/ha) and subjected to four different post-harvest

treatments with a 2.01 lb ai/gal (240g ai/L) SC formulation individual sample (and per-trial average) residues in/on apple and pear, respectively, were: 0.584-1.36 ppm (0.594-1.12 ppm) and 0.592-1.06 ppm (0.658-1.06 ppm) following dip treatment for 30 ± 3 seconds at 0.25 lb ai/100 gal (0.30 g ai/L) water; 0.496-0.261 ppm (0.556-2.59 ppm) and 0.696-1.37 ppm (0.764-1.30 ppm) following drench treatment for 30 ± 3 seconds at 0.25-0.27 lb ai/100 gal (0.30-0.32 g ai/L) water; 0.467-1.41 ppm (0.560-1.39 ppm) and 0.381-1.17 ppm (0.390-1.11 ppm) following spray treatment with 0.24-0.26 lb ai/200,000 lb fruit (12.0-13.0 g ai/10,000 kg fruit) in water + wax/oil; and 0.924-2.38 ppm (1.12-2.26 ppm) and 0.868-1.62 ppm (0.984-1.61 ppm) following the combined dip + spray treatments at the above noted rates.

An acceptable method was used for residue quantitation, and adequate storage stability data are available to support sample storage durations and conditions for the analyte.

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